

FILE 'CAPLUS' ENTERED AT 14:08:12 ON 20 JUN 2003

L3 7 S (HISTAMINE OR IMIDAZOLE 4 ETHYLAMINE OR ERAMIN OR IMIDAZOL 4

=> d que

L3 7 SEA FILE=CAPLUS (HISTAMINE OR IMIDAZOLE 4 ETHYLAMINE OR ERAMIN
OR IMIDAZOL 4 YL ETHYL AMINO) (5A) (BENZENESULFONAMIDE# OR
SULFAMIDE# OR SULFONYLAMIDO OR SULFONYL AMIDO OR AMINO
SULFONLYL OR SULFONYL AMINO)

=>

=> d 1-7 bib ab

L3 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2003 ACS

AN 2002:736933 CAPLUS

DN 137:247603

TI Preparation of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as histamine-3 receptor ligands for treatment of Alzheimer's disease, ADHD, epilepsy, narcolepsy, and obesity

IN Bennani, Youssef L.; Faghih, Ramin; Dwight, Wesley J.; Vasudevan, Anil; Conner, Scott E.

PA USA

SO U.S. Pat. Appl. Publ., 62 pp., Cont.-in-part of U.S. Ser. No. 902,925.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002137931	A1	20020926	US 2002-44471	20020111
	US 2002035103	A1	20020321	US 2001-902925	20010711
	US 6515013	B2	20030204		
PRAI	US 2000-218084P	P	20000713		
	US 2001-902925	A2	20010711		

OS MARPAT 137:247603

AB Title compds. I [wherein Z = a bond or CH₂; R₁ = OR₂, NR₃R₄, or 3-R₅-4-R₆-2,5-dioxoimidazolidinyl; R₂ = H, alkoxy-carbonyl, alkyl(carbonyl), aminocarbonyl, sulfono, or phosphono; R₃ and R₄ = independently H, alkenyl(sulfonyl), alkenyl(oxy)carbonyl, alkoxy-carbonyl, alkyl(sulfonyl), alkylcarbonyl, aminocarbonyl, aminosulfonyl, alkynyl(sulfonyl), alkynyl(oxy)carbonyl, (un)substituted (hetero)arylalkyl, or (hetero)arylalkenylcarbonyl, etc.; R₅, R₆, and R₇ = independently H or alkyl; or R₁ and R₇ together form =O; R₈ = (cyclo)alkylcarbonyl, (un)substituted aryl(carbonyl), arylcarbonylaryl, arylcarbonylheterocyclyl, cycloalkylcarbonylaryl, cycloalkylcarbonylheterocyclyl, heterocyclyl(carbonyl), heterocyclylcarbonylaryl, or heterocyclylcarbonylheterocyclyl; R₉ = H or alkyl; RA, RB, RC, and RD = independently H, alkenyl, alkoxy(alkoxy), (alkoxy)alkyl, alkoxy-carbonyl, alkylcarbonyl(oxy), alkylsulfinyl, alkylsulfonyl, alkylthio, alkynyl, amino(alkyl), aminocarbonyl, (carboxy)alkyl, (cyano)alkyl, formyl, halo(alkoxy), haloalkyl, (hydroxy)alkyl, SH, or NO₂, etc.; and pharmaceutically acceptable salts] were prepd. as histamine-3 receptor ligands. For example, 4'-[3-[(3R)-3-aminopyrrolidinyl]propoxy][1,1'-biphenyl]-4-carbonitrile in CH₂Cl₂ was treated with polymer supported N,N-diisopropylethylamine, catalytic amt. of DMAP, and 4-methoxybenzenesulfonyl chloride. After shaking at ambient temp. for 14 h, the mixt. was treated with tris(2-aminoethyl)amine-polystyrene resin and the mixt. shaken for an addnl. 2 h to give the [[(biphenyloxy)propyl]pyrrolidinyl]benzenesulfonamide II (79%). The latter bound to the histamine-3 receptor with K_i of 12 nM. I are useful for the treatment of acute myocardial infarction, asthma, bipolar disorder, cognitive enhancement, cutaneous carcinoma, depression, gastrointestinal disorders, inflammation, jet lag, medullary thyroid carcinoma, melanoma, Meniere's disease, migraine, motion sickness, obesity, pain, Parkinson's disease, schizophrenia, seizures, septic shock, Tourette's syndrome, Vertigo, wakefulness, Alzheimer's disease, attention-deficit hyperactivity disorder (ADHD), epilepsy, and narcolepsy (no data).

L3 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2003 ACS

AN 2002:221215 CAPLUS

DN 136:263087

TI Preparation of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as histamine-3 receptor ligands for treatment of Alzheimer's disease, ADHD, epilepsy, and narcolepsy

IN Bennani, Youssef L.; Faghih, Ramin; Dwight, Wesley J.; Vasudevan, Anil;
Conner, Scott E.

PA USA

SO U.S. Pat. Appl. Publ., 54 pp.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002035103	A1	20020321	US 2001-902925	20010711
	US 6515013	B2	20030204		
	US 2002137931	A1	20020926	US 2002-44471	20020111
PRAI	US 2000-218084P	P	20000713		
	US 2001-902925	A2	20010711		

OS MARPAT 136:263087

AB Title compds. I [wherein Z = a bond or CH₂; R₁ = OR₂, NR₃R₄, or substituted 2,5-dioxoimidazolidinyl; R₂ = H, alkoxy-carbonyl, alkyl(carbonyl), aminocarbonyl, sulfono, or phosphono; R₃ and R₄ = independently H, alkenyl(sulfonyl), alkenyl(oxy)carbonyl, alkoxy-carbonyl, alkyl(sulfonyl), alkylcarbonyl, aminocarbonyl, aminosulfonyl, alkynyl(sulfonyl), alkynyl(oxy)carbonyl, or (un)substituted (hetero)arylalkyl, (hetero)arylalkenylcarbonyl, etc.; R₇ = H or alkyl; or R₁ and R₇ together form :O; R₈ = (cyclo)alkylcarbonyl, or (un)substituted aryl(carbonyl), arylcarbonylaryl, arylcarbonylheterocyclyl, cycloalkylcarbonylaryl, cycloalkylcarbonylheterocyclyl, heterocyclyl(carbonyl), heterocyclylcarbonylaryl, or heterocyclylcarbonylheterocyclyl; R₉ = H or alkyl] were prepd. as histamine-3 receptor ligands. For example, 4'-[3-[(3R)-3-aminopyrrolidinyl]propoxy][1,1'-biphenyl]-4-carbonitrile in CH₂Cl₂ was treated with polymer supported N,N-diisopropylethylamine, catalytic N,N-dimethylaminopyridine, and 4-methoxybenzenesulfonyl chloride. After shaking at ambient temp. for 14 h, the mixt. was treated with tris(2-aminoethyl)amine-polystyrene resin and the mixt. shaken for an addnl. 2 h to give the [[(biphenyloxy)propyl]pyrrolidinyl]benzenesulfonamide II (79%). The latter bound to the histamine-3 receptor with K_i of 12 nM. I are useful for the treatment of acute myocardial infarction, asthma, cutaneous carcinoma, depression, inflammation, medullary thyroid carcinoma, melanoma, Meniere's disease, migraine, motion sickness, obesity, pain, Parkinson's disease, schizophrenia, seizures, septic shock, Alzheimer's disease, attention-deficit hyperactivity disorder (ADHD), epilepsy, and narcolepsy.

L3 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2003 ACS

AN 1999:737587 CAPLUS

DN 132:87751

TI 4-Chlorobenzyl sulfonamide and **sulfamide** derivatives of **histamine** homologues: the design of potent histamine H₃ receptor antagonists

AU Tozer, Matthew J.; Buck, Ildiko M.; Cooke, Tracey; Kalindjian, S. Barret; McDonald, Iain M.; Pether, Michael J.; Steel, Katherine I. M.

CS The James Black Foundation, London, SE24 9JE, UK

SO Bioorganic & Medicinal Chemistry Letters (1999), 9(21), 3103-3108
CODEN: BMCLE8; ISSN: 0960-894X

PB Elsevier Science Ltd.

DT Journal

LA English

AB 4-Chlorophenylmethanesulfonamide and (4-chlorobenzyl)**sulfamide** derivs. of **histamine** homologues were prepd. and found to be potent and selective histamine H₃ receptor antagonists. High receptor affinity and low differences in the data from the bioassays were achieved with the imidazol-4-ylbutyl analogs.

RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2003 ACS
 AN 1999:504279 CAPLUS
 DN 131:286325
 TI Novel carbonic anhydrase isozymes I, II and IV activators incorporating sulfonyl-histamino moieties
 AU Briganti, Fabrizio; Scozzafava, Andrea; Supuran, Claudiu T.
 CS Universita degli Studi, Laboratorio di Chimica Inorganica e Bioinorganica, Florence, 50121, Italy
 SO Bioorganic & Medicinal Chemistry Letters (1999), 9(14), 2043-2048
 CODEN: BMCLE8; ISSN: 0960-894X
 PB Elsevier Science Ltd.
 DT Journal
 LA English
 AB **Sulfonylamido**(ureido) derivs. of **histamine** were synthesized by an original procedure in order to obtain tight-binding activators of the zinc enzyme carbonic anhydrase (CA), exploiting the binding energy of the alkyl/arylsulfonyl moieties with amino acid residues at the entrance of the active site. In contrast to the lead mol., histamine, the new derivs. possessed higher affinity for three different CA isoenzymes, as evidenced by comparing the affinity consts. of these compds. for isoenzyme CA II.

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2003 ACS
 AN 1998:606886 CAPLUS
 DN 129:290093
 TI Novel H3 receptor antagonists. Sulfonamide homologs of histamine
 AU Wolin, Ronald; Connolly, Michael; Afonso, Adriano; Hey, John A.; She, Hoyan; Rivelli, Maria A.; Williams, Shirley M.; West, Robert E., Jr.
 CS Department of Chemistry, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA
 SO Bioorganic & Medicinal Chemistry Letters (1998), 8(16), 2157-2162
 CODEN: BMCLE8; ISSN: 0960-894X
 PB Elsevier Science Ltd.
 DT Journal
 LA English
 OS CASREACT 129:290093
 AB Sulfonamides derived from 4(5)-(omega.-aminoalkyl)-1H-imidazoles contg. chain lengths of three- to five-carbons were synthesized. Good to moderate H3 receptor binding affinities were obsd. for several Bu and pentyl homologs, whereas binding affinities were considerably weaker in the Pr series. Sepn. of the imidazole ring and the sulfonamide unit by a four- or five-carbon tether afforded potent H3 receptor antagonists.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

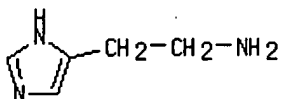
L3 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS
 AN 1982:193208 CAPLUS
 DN 96:193208
 TI Comparison of airway obstruction induced by propranolol and YM-09538 (a combined .alpha.- and .beta.-adrenoceptor blocking drug)
 AU Tomioka, K.; Yamada, T.; Takenaka, T.
 CS Cent. Res. Lab., Yamanouchi Pharm. Co. Ltd., Tokyo, 174, Japan
 SO Archives Internationales de Pharmacodynamie et de Therapie (1982), 256(1), 97-107
 CODEN: AIPTAK; ISSN: 0003-9780
 DT Journal
 LA English
 AB In the isolated guinea-pig right atria and tracheal strips, both dl-propranolol (I) [13013-17-7] and YM-09538 (II) [70958-86-0] caused a parallel shift of the dose-response curve for isoproterenol to the right, indicating that these 2 drugs block nonselectively the .beta.1- and

.beta.2-adrenoceptors. Propranolol potentiated the histamine [51-45-6]-induced bronchoconstriction in the anesthetized dogs, whereas YM-09538 did not affect the histamine-induced bronchoconstriction. Propranolol degranulated the isolated rat mesenteric mast cells in contrast to YM-09538 which had no significant effect on mast cells. Neither propranolol nor YM-09538 affected the hapten-specific IgE antibody response in female BDF1 mice. Apparently, YM-09538 has a much lesser effect on airway function than propranolol.

L3 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2003 ACS
AN 1964:63800 CAPLUS
DN 60:63800
OREF 60:11257e
TI Ways of overcoming insulin resistance in patients with diabetes mellitus
AU Kamysheva, E. P.
SO Vopr. Neiroendokrinol. Patol., Gorki, Sb. (1963) 254-7
From: Ref. Zh., Biol. Khim. 1963, Abstr. No. 22F-1353.
DT Journal
LA Unavailable
AB Administration of hyaluronidase, **histamine**, hexonium, and **sulfamide** prepns. and needle pricking were effective in overcoming resistance to insulin in diabetics.

=>

RN 51-45-6 REGISTRY
 CN 1H-Imidazole-4-ethanamine (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN Histamine (8CI)
 OTHER NAMES:
 CN β -Imidazolyl-4-ethylamine
 CN 2-(1H-Imidazol-4-yl)ethanamine
 CN 2-(1H-Imidazol-4-yl)ethylamine
 CN 2-(1H-Imidazol-5-yl)ethylamine
 CN 2-(4-Imidazolyl)ethanamine
 CN 2-(4-Imidazolyl)ethylamine
 CN 4-(2-Aminoethyl)imidazole
 CN 5-Imidazoleethylamine
 CN Eramin
 CN Ergamine
 CN Ergotidine
 CN Imidazole-4-ethylamine
 FS 3D CONCORD
 MF C5 H9 N3
 CI COM
 LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*,
 BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS,
 CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM,
 CSNB, DDFU, DIOGENES, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, GMELIN*,
 HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS,
 NAPRALERT, NIOSHTIC, PHARMASEARCH, PIRA, PROMT, RTECS*, SPECINFO,
 SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
 (*File contains numerically searchable property data)
 Other Sources: DSL**, EINECS**, TSCA**
 (**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

31050 REFERENCES IN FILE CA (1957 TO DATE)
 386 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 31060 REFERENCES IN FILE CAPLUS (1957 TO DATE)
 10 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

* * * * * Welcome to STN International * * * * *

<u>NEWS 1</u>		Web Page URLs for STN Seminar Schedule - N. America
<u>NEWS 2</u>		"Ask CAS" for self-help around the clock
<u>NEWS 3</u>	Jun 03	New e-mail delivery for search results now available
<u>NEWS 4</u>	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
<u>NEWS 5</u>	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
<u>NEWS 6</u>	Aug 26	Sequence searching in REGISTRY enhanced
<u>NEWS 7</u>	Sep 03	JAPIO has been reloaded and enhanced
<u>NEWS 8</u>	Sep 16	Experimental properties added to the REGISTRY file
<u>NEWS 9</u>	Sep 16	CA Section Thesaurus available in CAPLUS and CA
<u>NEWS 10</u>	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
<u>NEWS 11</u>	Oct 24	BEILSTEIN adds new search fields
<u>NEWS 12</u>	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
<u>NEWS 13</u>	Nov 18	DKILIT has been renamed APOLLIT
<u>NEWS 14</u>	Nov 25	More calculated properties added to REGISTRY
<u>NEWS 15</u>	Dec 04	CSA files on STN
<u>NEWS 16</u>	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
<u>NEWS 17</u>	Dec 17	TOXCENTER enhanced with additional content
<u>NEWS 18</u>	Dec 17	Adis Clinical Trials Insight now available on STN
<u>NEWS 19</u>	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
<u>NEWS 20</u>	Feb 13	CANCERLIT is no longer being updated
<u>NEWS 21</u>	Feb 24	METADEx enhancements
<u>NEWS 22</u>	Feb 24	PCTGEN now available on STN
<u>NEWS 23</u>	Feb 24	TEMA now available on STN
<u>NEWS 24</u>	Feb 26	NTIS now allows simultaneous left and right truncation
<u>NEWS 25</u>	Feb 26	PCTFULL now contains images
<u>NEWS 26</u>	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
<u>NEWS 27</u>	Mar 20	EVENTLINE will be removed from STN
<u>NEWS 28</u>	Mar 24	PATDPAFULL now available on STN
<u>NEWS 29</u>	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
<u>NEWS 30</u>	Apr 11	Display formats in DGENE enhanced
<u>NEWS 31</u>	Apr 14	MEDLINE Reload
<u>NEWS 32</u>	Apr 17	Polymer searching in REGISTRY enhanced
<u>NEWS 33</u>	Jun 13	Indexing from 1947 to 1956 added to records in CA/CAPLUS
<u>NEWS 34</u>	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
<u>NEWS 35</u>	Apr 28	RDISCLOSURE now available on STN
<u>NEWS 36</u>	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
<u>NEWS 37</u>	May 15	MEDLINE file segment of TOXCENTER reloaded
<u>NEWS 38</u>	May 15	Supporter information for ENCOMPAT and ENCOMPLIT updated
<u>NEWS 39</u>	May 16	CHEMREACT will be removed from STN
<u>NEWS 40</u>	May 19	Simultaneous left and right truncation added to WSCA
<u>NEWS 41</u>	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
<u>NEWS 42</u>	Jun 06	Simultaneous left and right truncation added to CBNB
<u>NEWS 43</u>	Jun 06	PASCAL enhanced with additional data
<u>NEWS EXPRESS</u>		April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
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NEWS WWW CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 06:05:56 ON 20 JUN 2003

=> file caplus
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.21	0.21

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 06:06:21 ON 20 JUN 2003
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FILE COVERS 1907 - 20 Jun 2003 VOL 138 ISS 26
FILE LAST UPDATED: 19 Jun 2003 (20030619/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> e dementia/ct

E#	FREQUENCY	AT	TERM
E1	0	2	DEMBER PHOTOVOLTAIC EFFECT/CT
E2	0	2	DEMECOLCINE/CT
E3	0	2	--> DEMENTIA/CT
E4	0	2	DEMENTIA MENTAL DISORDER/CT
E5	0	2	DEMENTIA PRAECOX/CT
E6	0	2	DEMENTIA WITH LEWY BODIES/CT
E7	0	1	DEMERARAE/CT
E8	0	1	DEMERARANUM/CT
E9	194	2	DEMERCURATION/CT
E10	10	3	DEMERCURATION CATALYSTS/CT
E11	1		DEMERECE/CT
E12	1		DEMERECE, MILISLAV/CT

=> e e3+/ct

'+' IS NOT VALID HERE

For an explanation of the EXPAND command, enter "HELP EXPAND" at an arrow prompt (=>).

=> d e3+/ct

'E3+' MUST END IN '/Q', '/A', '/L', '/S' OR '/B'

The saved name for a query (or structure or screen set) must end with '/Q'. The saved name for an answer set must end with '/A'. The saved name for an L# list must end with '/L'. SDI request names must end with '/S'. To see a list of all saved query, answer set,, and L# list names for this loginid, enter "DISPLAY SAVED" at an arrow prompt (=>). Enter "DISPLAY SAVED/S" to see a list of SDI request names. Enter "DISPLAY SAVED/B" to see a list of BATCH search requests.

=> file caplus wpids medline embase

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.83

1.04

FILE 'CAPLUS' ENTERED AT 06:07:28 ON 20 JUN 2003

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FILE 'WPIDS' ENTERED AT 06:07:28 ON 20 JUN 2003

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FILE 'MEDLINE' ENTERED AT 06:07:28 ON 20 JUN 2003

FILE 'EMBASE' ENTERED AT 06:07:28 ON 20 JUN 2003

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=> s dementia or alzheimer?

L1 172320 DEMENTIA OR ALZHEIMER?

=> s l1 or neurodegenerat? disease#

L2 182615 L1 OR NEURODEGENERAT? DISEASE#

=> s ((sulfonylamido or sulfonyl amido) (2a) histamine) or nsaid or non steroidal (a MISSING OPERATOR 'STEROIDAL (ANTIINFLAM'

The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

=> s ((sulfonylamido or sulfonyl amido) (2a) histamine) or nsaid or ((non steroidal UNMATCHED RIGHT PARENTHESIS 'ESTROGEN)'

The number of right parentheses in a query must be equal to the number of left parentheses.

=> s ((sulfonylamido or sulfonyl amido) (2a) histamine) or nsaid or ((non steroidal

* * * * * RECONNECTED TO STN INTERNATIONAL * * * * *

SESSION RESUMED IN FILE 'CAPLUS, WPIDS, MEDLINE, EMBASE'

AT 06:15:49 ON 20 JUN 2003

FILE 'CAPLUS' ENTERED AT 06:15:49 ON 20 JUN 2003

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FILE 'WPIDS' ENTERED AT 06:15:49 ON 20 JUN 2003

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FILE 'MEDLINE' ENTERED AT 06:15:49 ON 20 JUN 2003

FILE 'EMBASE' ENTERED AT 06:15:49 ON 20 JUN 2003

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COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

60.51

61.55

=> d his

(FILE 'HOME' ENTERED AT 06:05:56 ON 20 JUN 2003)

FILE 'CAPLUS' ENTERED AT 06:06:21 ON 20 JUN 2003

E DEMENTIA/CT

FILE 'CAPLUS, WPIDS, MEDLINE, EMBASE' ENTERED AT 06:07:28 ON 20 JUN 2003

L1 172320 S DEMENTIA OR ALZHEIMER?

L2 182615 S L1 OR NEURODEGENERAT? DISEASE#

L3 1127914 S ((SULFONYLAMIDO OR SULFONYL AMIDO) (2A) HISTAMINE) OR NSAID O

=> s 12 (1) 13

L4 3550 L2 (L) L3

=> s 14 and ((sulfonylamido (5a) histamine) or (sulfonyl (5a) amido (5a) histamine))

L5 0 L4 AND ((SULFONYLAMIDO (5A) HISTAMINE) OR (SULFONYL (5A) AMIDO (5A) HISTAMINE))

=> s 14 and histamine

L6 24 L4 AND HISTAMINE

=> s 12 and histamine

L7 496 L2 AND HISTAMINE

=> s 17 and (histamine (10a) sulfonyl)

L8 3 L7 AND (HISTAMINE (10A) SULFONYL)

=> d 1-3 bib hit

L8 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS

Full Text	Citing References
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AN 2002:781497 CAPLUS

DN 137:262957

TI Preparation of aryloxyalkylamines as histamine H3 receptor modulators

IN Schwartz, Jean-Charles; Arrang, Jean-Michel; Garbarg, Monique; Lecomte, Jeanne-Marie; Ligneau, Xavier; Schunack, Walter G.; Stark, Holger; Ganellin, Charon Robin; Leurquin, Fabien; Sigurd, Elz

PA Societe Civile Bioprojet, Fr.

SO PCT Int. Appl., 195 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006254	A2	20000210	WO 1999-EP5744	19990729
WO 2000006254	A3	20000504		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,

TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AM, AZ, BY, KG, KZ, MD,
 RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT,
 LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR,
 NE, SN, TD, TG

EP 978512 A1 20000209 EP 1998-401944 19980729
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 IE, SI, LT, LV, FI, RO

EP 982300 A2 20000301 EP 1998-403351 19981231
 EP 982300 A3 20000308
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 IE, SI, LT, LV, FI, RO

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 AU 9955119 A1 20000221 AU 1999-55119 19990729
 EP 1100503 A2 20010523 EP 1999-941543 19990729
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TI Preparation of aryloxyalkylamines as **histamine** H3 receptor modulators

AB The title non-imidazole compds. I [wherein n = 2-8; m = 0-5; X = O, S; R1,
 R2 = alkyl, cycloalkyl; NR1R2 = (unsatd.) N-contg. ring, substituted
 piperazino; R3 = halo, alkyl, cycloalkyl, CF3, aryl, alkoxy, aryloxy, NO2,
 CHO, alkanoyl, aroyl, aralkanoyl, amino, carboxamido, cyano, alkoximino,
 alkenyl, alkynyl, etc.; and their pharmaceutically acceptable salts,
 hydrates, polymorphic cryst. structures, optical isomers, racemates,
 diastereoisomers, and enantiomers] were prepd. as antagonists and/or
 agonists of the **histamine** H3-receptors. Thus, 1-[3-(4-
 cyanophenoxy)prgl67opyl]piperidine hydrogen oxalate (general prepn. given)
 increased telemethylhistamine in mice with ED50 = 0.20 mg/kg orally. I
 are useful for the treatment of central nervous system disorders, in
 particular **Alzheimer's** disease, mood and attention alterations,
 cognitive deficits in psychiatric pathologies, obesity, vertigo, and
 motion sickness (no data).

ST aryloxyalkylamine prepn **histamine** receptor antagonist agonist;
 azaheterocycloalkoxybenzene nonimidazole prepn **histamine** receptor
 antagonist agonist; nootropic aryloxyalkylamine; antiobesity agent
 aryloxyalkylamine; pyschotropic aryloxyalkylamine; memory enhancer
 aryloxyalkylamine; motion sickness treatment aryloxyalkylamine

IT Intestine, disease
 (Crohn's; prepn. of aryloxyalkylamines as **histamine** H3
 receptor modulators)

IT Antihistamines
 (H3; prepn. of aryloxyalkylamines as **histamine** H3 receptor
 modulators)

IT Mental disorder
 (attention deficit disorder; prepn. of aryloxyalkylamines as
histamine H3 receptor modulators)

IT Mental activity
 (attention, stimulators; prepn. of aryloxyalkylamines as
histamine H3 receptor modulators)

IT Bronchi
 (bronchitis; prepn. of aryloxyalkylamines as **histamine** H3
 receptor modulators)

IT Eye, disease
 (conjunctivitis; prepn. of aryloxyalkylamines as **histamine** H3
 receptor modulators)

IT Bladder
(cystitis; prepn. of aryloxyalkylamines as **histamine H3** receptor modulators)

IT Mental disorder
(depression; prepn. of aryloxyalkylamines as **histamine H3** receptor modulators)

IT Urogenital tract
(diseases, inflammation; prepn. of aryloxyalkylamines as **histamine H3** receptor modulators)

IT Intestine, disease
(duodenum, ulcer; prepn. of aryloxyalkylamines as **histamine H3** receptor modulators)

IT Uterus, disease
(endometritis; prepn. of aryloxyalkylamines as **histamine H3** receptor modulators)

IT Digestive tract
(gastroenteritis; prepn. of aryloxyalkylamines as **histamine H3** receptor modulators)

IT Bladder
Defecation
(incontinence; prepn. of aryloxyalkylamines as **histamine H3** receptor modulators)

IT Heart, disease
(infarction, therapeutic agents; prepn. of aryloxyalkylamines as **histamine H3** receptor modulators)

IT Heart, disease
(infarction; prepn. of aryloxyalkylamines as **histamine H3** receptor modulators)

IT Eye, disease
Respiratory tract
(inflammation; prepn. of aryloxyalkylamines as **histamine H3** receptor modulators)

IT Intestine, disease
(irritable bowel syndrome; prepn. of aryloxyalkylamines as **histamine H3** receptor modulators)

IT Headache
(migraine; prepn. of aryloxyalkylamines as **histamine H3** receptor modulators)

IT Mental disorder
(mood-affecting; prepn. of aryloxyalkylamines as **histamine H3** receptor modulators)

IT Ovarian cycle
(premenstrual syndrome; prepn. of aryloxyalkylamines as **histamine H3** receptor modulators)

IT Allergy inhibitors
Alzheimer's disease
Analgesics
Anti-Alzheimer's agents
Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Antidepressants
Antimigraine agents
Antiobesity agents
Antiulcer agents
Anxiolytics
Arthritis
Asthma
Cognition enhancers
Dermatitis

Dizziness
 Heart, disease
 Human
 Hypnotics and Sedatives
 Nervous system agents
 Pruritus
 Psychotropics
 Stress, animal
 Urticaria
 (prepn. of aryloxyalkylamines as histamine H3 receptor modulators)

- IT Nose
 (rhinitis; prepn. of aryloxyalkylamines as histamine H3 receptor modulators)
- IT Memory, biological
 (stimulators; prepn. of aryloxyalkylamines as histamine H3 receptor modulators)
- IT Bronchi
 Trachea (anatomical)
 (tracheobronchitis; prepn. of aryloxyalkylamines as histamine H3 receptor modulators)
- IT Motion sickness
 (treatment; prepn. of aryloxyalkylamines as histamine H3 receptor modulators)
- IT Stomach, disease
 (ulcer; prepn. of aryloxyalkylamines as histamine H3 receptor modulators)
- IT Intestine, disease
 (ulcerative colitis; prepn. of aryloxyalkylamines as histamine H3 receptor modulators)
- IT 23999-21-5P, 1-Propanamine, N,N-diethyl-3-(4-nitrophenoxy)- 27078-39-3P
 46843-28-1P, Benzonitrile, 4-[3-(diethylamino)propoxy]- 46926-57-2P,
 Benzonitrile, 4-[4-(diethylamino)butoxy]- 49773-11-7P, Benzonitrile,
 4-[2-(diethylamino)ethoxy]- 70403-69-9P, 5-Piperidinopentylamine
 77427-42-0P 82625-46-5P, Benzaldehyde, 4-[3-(1-piperidinyl)propoxy]-
 86355-72-8P, Piperidine, 1-(5-phenoxypropyl)- 92322-18-4P, Pyrrolidine,
 1-(4-phenoxybutyl)- 92374-75-9P, 1-[3-(4-Nitrophenoxy)propyl]piperidine
 93699-55-9P, 1-Propanone, 1-[4-[3-(diethylamino)propoxy]phenyl]-
 99759-00-9P 116871-18-2P, Pyrrolidine, 1-(3-phenoxypropyl)-
 146440-15-5P, Benzonitrile, 4-[3-(dimethylamino)propoxy]- 146440-20-2P,
 Benzonitrile, 4-[3-(1-piperidinyl)propoxy]- 164029-23-6P, Benzonitrile,
 4-[[5-(1-piperidinyl)pentyl]oxy]- 169815-42-3P, 7-Chloro-4-(3-
 piperidinopropylamino)quinoline 172018-41-6P 199920-60-0P
 220727-93-5P, 1-Pentanamine, N-ethyl-N-methyl-5-phenoxy- 220727-94-6P,
 1-Pentanamine, N-ethyl-N-methyl-5-phenoxy-, ethanedioate (1:1)
 220727-95-7P, 1-Pentanamine, N-ethyl-5-phenoxy-N-propyl- 220727-96-8P,
 1-Pentanamine, N-ethyl-5-phenoxy-N-propyl-, ethanedioate (1:1)
 220727-99-1P, Pyrrolidine, 1-(5-phenoxypropyl)- 220728-00-7P,
 Pyrrolidine, 1-(5-phenoxypropyl)-, ethanedioate (1:1) 220728-01-8P,
 Piperidine, 1-(5-phenoxypropyl)-, ethanedioate (1:1) 220728-02-9P,
 1H-Azepine, hexahydro-1-(5-phenoxypropyl)- 220728-03-0P, 1H-Azepine,
 hexahydro-1-(5-phenoxypropyl)-, ethanedioate (1:1) 220728-04-1P,
 Morpholine, 4-(5-phenoxypropyl)- 220728-05-2P, Morpholine,
 4-(5-phenoxypropyl)-, ethanedioate (1:1) 220728-07-4P, Pyrrolidine,
 1-[5-(4-fluorophenoxy)pentyl]- 220728-08-5P, Pyrrolidine,
 1-[5-(4-fluorophenoxy)pentyl]-, ethanedioate (1:1) 220728-09-6P,
 Pyrrolidine, 1-[5-(4-chlorophenoxy)pentyl]- 220728-10-9P, Pyrrolidine,
 1-[5-(4-chlorophenoxy)pentyl]-, ethanedioate (1:1) 220728-11-0P,
 Pyrrolidine, 1-[5-(3-chlorophenoxy)pentyl]- 220728-12-1P, Pyrrolidine,
 1-[5-(3-chlorophenoxy)pentyl]-, ethanedioate (1:1) 220728-13-2P,

Benzenamine, 4-[[5-(1-pyrrolidinyl)pentyl]oxy]- 220728-15-4P,
 Pyrrolidine, 1-[5-(4-methylphenoxy)pentyl]- 220728-16-5P, Pyrrolidine,
 1-[5-(4-methylphenoxy)pentyl]-, ethanedioate (1:1) 220728-17-6P,
 Pyrrolidine, 1-[5-(4-nitrophenoxy)pentyl]- 220728-18-7P, Pyrrolidine,
 1-[5-(4-nitrophenoxy)pentyl]-, ethanedioate (1:1) 220728-19-8P,
 Pyrrolidine, 1-[5-(3-nitrophenoxy)pentyl]- 220728-20-1P, Pyrrolidine,
 1-[5-(3-nitrophenoxy)pentyl]-, ethanedioate (1:1) 220728-21-2P,
 Benzonitrile, 4-[[5-(1-pyrrolidinyl)pentyl]oxy]- 220728-23-4P,
 Benzonitrile, 3-[[5-(1-pyrrolidinyl)pentyl]oxy]- 220728-24-5P,
 Benzonitrile, 3-[[5-(1-pyrrolidinyl)pentyl]oxy]-, ethanedioate (1:1)
256952-10-0P, Piperidine, 2-methyl-1-(5-phenoxy)pentyl]- 256952-11-1P,
 Piperidine, 1-(5-phenoxy)pentyl)-4-propyl- 256952-12-2P, Piperidine,
 4-methyl-1-(5-phenoxy)pentyl)- 256952-13-3P, Piperidine,
 3-methyl-1-(5-phenoxy)pentyl)- 256952-14-4P, Piperazine,
 1-acetyl-4-(5-phenoxy)pentyl)- 256952-15-5P, Piperidine,
 3,5-dimethyl-1-(5-phenoxy)pentyl)-, (3R,5R)-rel- 256952-16-6P,
 Piperidine, 3,5-dimethyl-1-(5-phenoxy)pentyl)-, (3R,5S)-rel-
256952-17-7P, Piperidine, 2,6-dimethyl-1-(5-phenoxy)pentyl)-, (2R,6S)-rel-
256952-18-8P, 4-Piperidinecarboxylic acid, 1-(5-phenoxy)pentyl)-, ethyl
 ester 256952-19-9P, 3-Piperidinecarboxylic acid, 1-(5-phenoxy)pentyl)-,
 ethyl ester 256952-20-2P, Pyridine, 1,2,3,6-tetrahydro-1-(5-
 phenoxy)pentyl)- 256952-21-3P, Pyrrolidine, 1-[5-(4-
 methoxyphenoxy)pentyl]- 256952-22-4P, Pyrrolidine, 1-[5-(2-
 naphthalenyloxy)pentyl]- 256952-23-5P, Pyrrolidine, 1-[5-(1-
 naphthalenyloxy)pentyl]- 256952-24-6P, Pyrrolidine, 1-[5-([1,1'-
 biphenyl]-4-yloxy)pentyl]- 256952-25-7P, Pyrrolidine,
 1-[5-[(5,6,7,8-tetrahydro-2-naphthalenyl)oxy]pentyl]- 256952-26-8P,
 Pyrrolidine, 1-[5-([1,1'-biphenyl]-3-yloxy)pentyl]- 256952-27-9P,
 1H-Pyrrole, 2,5-dihydro-1-(5-phenoxy)pentyl)- 256952-28-0P, Pyrrolidine,
 1-[5-[(5,6,7,8-tetrahydro-1-naphthalenyl)oxy]pentyl]- 256952-29-1P,
 Pyrrolidine, 1-(6-phenoxyhexyl)- 256952-30-4P, Piperidine,
 3-methyl-1-[5-(4-nitrophenoxy)pentyl]- 256952-31-5P, Ethanone,
 1-[4-[[5-(1-pyrrolidinyl)pentyl]oxy]phenyl]- 256952-32-6P, Methanone,
 phenyl[4-[[5-(1-pyrrolidinyl)pentyl]oxy]phenyl]- 256952-34-8P, Ethanone,
 2-phenyl-1-[4-[[5-(1-pyrrolidinyl)pentyl]oxy]phenyl]- 256952-36-0P,
 Acetamide, N-[4-[[5-(1-pyrrolidinyl)pentyl]oxy]phenyl]- 256952-38-2P,
 Pyrrolidine, 1-[5-(4-phenoxyphenoxy)pentyl]- 256952-41-7P, Benzamide,
 N-[4-[[5-(1-pyrrolidinyl)pentyl]oxy]phenyl]- 256952-43-9P,
 Benzenemethanol, α -methyl-4-[[5-(1-pyrrolidinyl)pentyl]oxy]-
256952-44-0P, Benzonitrile, 4-[[5-(diethylamino)pentyl]oxy]-
256952-45-1P, Benzonitrile, 4-[[5-(dimethylamino)pentyl]oxy]-
256952-46-2P, Benzonitrile, 4-[[5-(dipropylamino)pentyl]oxy]-
256952-48-4P, Benzonitrile, 4-[3-(1-pyrrolidinyl)propoxy]- 256952-49-5P,
 Benzonitrile, 4-[3-(hexahydro-1H-azepin-1-yl)propoxy]- 256952-51-9P,
 Benzonitrile, 4-[[6-(diethylamino)hexyl]oxy]- 256952-54-2P,
 Benzonitrile, 4-[3-(dipropylamino)propoxy]- 256952-57-5P,
 Benzenemethanol, 4-[3-(diethylamino)propoxy]- α -methyl-
256952-61-1P, Ethanone, 1-[4-[3-(diethylamino)propoxy]phenyl]-, oxime
256952-65-5P, Ethanone, 1-[4-[3-(1-piperidinyl)propoxy]phenyl]-
256952-69-9P, Ethanone, 1-[4-[3-(3-methyl-1-piperidinyl)propoxy]phenyl]-
256952-72-4P, Ethanone, 1-[4-[3-[(3R,5R)-3,5-dimethyl-1-
 piperidinyl]propoxy]phenyl]-, rel- 256952-76-8P, Ethanone,
 1-[4-[3-(4-methyl-1-piperidinyl)propoxy]phenyl]- 256952-78-0P,
 1-Propanone, 1-[4-[3-(1-piperidinyl)propoxy]phenyl]- 256952-81-5P,
 Ethanone, 1-[4-[3-[(3R,5S)-3,5-dimethyl-1-piperidinyl]propoxy]phenyl]-,
 rel- 256952-84-8P, 1-Propanone, 2-methyl-1-[4-[3-(1-
 piperidinyl)propoxy]phenyl]- 256952-87-1P, 1-Butanone,
 1-[4-[3-(1-piperidinyl)propoxy]phenyl]- 256952-89-3P, Ethanone,
 1-[4-[3-(3,6-dihydro-1(2H)-pyridinyl)propoxy]phenyl]- 256952-94-0P,
 Pyrrolidine, 1-[5-(phenylthio)pentyl]- 256952-95-1P, Pyrrolidine,

1-[4-(phenylthio)butyl]- 256952-96-2P, Ethanone, 1-[4-[3-(diethylamino)propoxy]phenyl]- 256953-01-2P, Piperidine, 2-methyl-1-(5-phenoxypropyl)-, ethanedioate (10:11) 256953-02-3P, Piperidine, 1-(5-phenoxypropyl)-4-propyl-, ethanedioate (1:1) 256953-03-4P, Piperidine, 4-methyl-1-(5-phenoxypropyl)-, ethanedioate (1:1) 256953-04-5P, Piperidine, 3-methyl-1-(5-phenoxypropyl)-, ethanedioate (1:1) 256953-05-6P, Piperazine, 1-acetyl-4-(5-phenoxypropyl)-, ethanedioate (1:1) 256953-06-7P, Piperidine, 3,5-dimethyl-1-(5-phenoxypropyl)-, (3R,5R)-rel-, ethanedioate (1:1) 256953-07-8P, Piperidine, 3,5-dimethyl-1-(5-phenoxypropyl)-, (3R,5S)-rel-, ethanedioate (1:1) 256953-08-9P, Piperidine, 2,6-dimethyl-1-(5-phenoxypropyl)-, hydrochloride, (2R,6S)-rel- 256953-09-0P, 4-Piperidinecarboxylic acid, 1-(5-phenoxypropyl)-, ethyl ester, ethanedioate (1:1) 256953-10-3P, 3-Piperidinecarboxylic acid, 1-(5-phenoxypropyl)-, ethyl ester, ethanedioate (1:1) 256953-11-4P, Pyridine, 1,2,3,6-tetrahydro-1-(5-phenoxypropyl)-, ethanedioate (1:1) 256953-12-5P, Pyrrolidine, 1-[5-(4-methoxyphenoxy)pentyl]-, ethanedioate (1:1) 256953-13-6P, Benzonitrile, 4-[[5-(1-pyrrolidinyl)pentyl]oxy]-, ethanedioate (10:11) 256953-14-7P, Pyrrolidine, 1-[5-(2-naphthalenyloxy)pentyl]-, ethanedioate (1:1) 256953-15-8P, Pyrrolidine, 1-[5-(1-naphthalenyloxy)pentyl]-, ethanedioate (4:5) 256953-16-9P, Pyrrolidine, 1-[5-([1,1'-biphenyl]-4-yloxy)pentyl]-, ethanedioate (1:1) 256953-17-0P, Pyrrolidine, 1-[5-([5,6,7,8-tetrahydro-2-naphthalenyl]oxy)pentyl]-, ethanedioate (1:1) 256953-18-1P, Pyrrolidine, 1-[5-([1,1'-biphenyl]-3-yloxy)pentyl]-, ethanedioate (10:11) 256953-19-2P, 1H-Pyrrole, 2,5-dihydro-1-(5-phenoxypropyl)-, ethanedioate (1:1) 256953-20-5P, Pyrrolidine, 1-[5-([5,6,7,8-tetrahydro-1-naphthalenyl]oxy)pentyl]-, ethanedioate (1:1) 256953-21-6P, Pyrrolidine, 1-(4-phenoxybutyl)-, ethanedioate (1:1) 256953-22-7P, Pyrrolidine, 1-(6-phenoxyhexyl)-, ethanedioate (10:11) 256953-23-8P, Pyrrolidine, 1-[5-(phenylthio)pentyl]-, ethanedioate (10:11) 256953-24-9P, Pyrrolidine, 1-[4-(phenylthio)butyl]-, ethanedioate (1:1) 256953-25-0P, Pyrrolidine, 1-(3-phenoxypropyl)-, ethanedioate (1:1) 256953-26-1P, Piperidine, 3-methyl-1-[5-(4-nitrophenoxy)pentyl]-, ethanedioate (1:1) 256953-27-2P, Ethanone, 1-[4-[[5-(1-pyrrolidinyl)pentyl]oxy]phenyl]-, ethanedioate (1:1) 256953-28-3P, Benzenamine, 4-[[5-(1-pyrrolidinyl)pentyl]oxy]-, ethanedioate (10:21) 256953-29-4P, 1-Propanamine, N,N-diethyl-3-(4-nitrophenoxy)-, ethanedioate (1:1) 256953-30-7P, Benzonitrile, 4-[3-(diethylamino)propoxy]-, ethanedioate (1:1) 256953-31-8P, Methanone, phenyl[4-[[5-(1-pyrrolidinyl)pentyl]oxy]phenyl]-, ethanedioate (1:1) 256953-32-9P, Ethanone, 2-phenyl-1-[4-[[5-(1-pyrrolidinyl)pentyl]oxy]phenyl]-, ethanedioate (1:1) 256953-33-0P, Ethanone, 1-[4-[3-(diethylamino)propoxy]phenyl]-, ethanedioate (10:11) 256953-34-1P, Acetamide, N-[4-[[5-(1-pyrrolidinyl)pentyl]oxy]phenyl]-, ethanedioate (1:1) 256953-35-2P, Pyrrolidine, 1-[5-(4-phenoxyphenoxy)pentyl]-, ethanedioate (1:1) 256953-36-3P, Benzamide, N-[4-[[5-(1-pyrrolidinyl)pentyl]oxy]phenyl]-, ethanedioate (10:11) 256953-37-4P, Benzenemethanol, α -methyl-4-[[5-(1-pyrrolidinyl)pentyl]oxy]-, ethanedioate (1:1) (salt) 256953-38-5P, Benzonitrile, 4-[[5-(diethylamino)pentyl]oxy]-, ethanedioate (1:1) 256953-39-6P, Benzonitrile, 4-[[5-(1-piperidinyl)pentyl]oxy]-, ethanedioate (1:1) 256953-40-9P, Benzonitrile, 4-[[5-(dimethylamino)pentyl]oxy]-, ethanedioate (1:1) 256953-41-0P, Benzonitrile, 4-[2-(diethylamino)ethoxy]-, ethanedioate (1:1) 256953-42-1P, Benzonitrile, 4-[3-(dimethylamino)propoxy]-, ethanedioate (1:1) 256953-43-2P, Benzonitrile, 4-[4-(diethylamino)butoxy]-, ethanedioate (1:1) 256953-44-3P, Benzonitrile, 4-[[5-(dipropylamino)pentyl]oxy]-, ethanedioate (1:1) 256953-45-4P, Benzonitrile, 4-[3-(1-pyrrolidinyl)propoxy]-, ethanedioate (10:11) 256953-46-5P, Benzonitrile,

4-[3-(1-piperidinyl)propoxy]-, ethanedioate (1:1) 256953-47-6P,
 Benzonitrile, 4-[3-(hexahydro-1H-azepin-1-yl)propoxy]-, ethanedioate (1:1)
256953-48-7P, Benzonitrile, 4-[[6-(diethylamino)hexyl]oxy]-, ethanedioate
 (1:1) 256953-49-8P, Benzonitrile, 4-[3-(dipropylamino)propoxy]-,
 ethanedioate (1:1) 256953-50-1P, Benzenemethanol, 4-[3-
 (diethylamino)propoxy]- α -methyl-, ethanedioate (1:1) (salt)
256953-51-2P, Ethanone, 1-[4-[3-(diethylamino)propoxy]phenyl]-, oxime,
 ethanedioate (1:1) 256953-52-3P, Ethanone, 1-[4-[3-(1-
 piperidinyl)propoxy]phenyl]-, ethanedioate (1:1) 256953-53-4P, Ethanone,
 1-[4-[3-(3-methyl-1-piperidinyl)propoxy]phenyl]-, ethanedioate (1:1)
256953-54-5P, Ethanone, 1-[4-[3-[(3R,5R)-3,5-dimethyl-1-
 piperidinyl]propoxy]phenyl]-, rel-, ethanedioate (1:1) 256953-55-6P,
 Ethanone, 1-[4-[3-(4-methyl-1-piperidinyl)propoxy]phenyl]-, ethanedioate
 (1:1) 256953-56-7P, 1-Propanone, 1-[4-[3-(1-piperidinyl)propoxy]phenyl]-,
 ethanedioate (1:1) 256953-58-9P, Ethanone, 1-[4-[3-[(3R,5S)-3,5-
 dimethyl-1-piperidinyl]propoxy]phenyl]-, rel-, ethanedioate (1:1)
256953-59-0P, Benzaldehyde, 4-[3-(1-piperidinyl)propoxy]-, ethanedioate
 (1:1) 256953-60-3P, 1-Propanone, 2-methyl-1-[4-[3-(1-
 piperidinyl)propoxy]phenyl]-, ethanedioate (1:1) 256953-61-4P,
 1-Propanone, 1-[4-[3-(diethylamino)propoxy]phenyl]-, ethanedioate (2:3)
256953-62-5P, 1-Butanone, 1-[4-[3-(1-piperidinyl)propoxy]phenyl]-,
 ethanedioate (1:1) 256953-63-6P, Ethanone, 1-[4-[3-(3,6-dihydro-1(2H)-
 pyridinyl)propoxy]phenyl]-, ethanedioate (10:11) 362665-49-4P
362665-51-8P 362665-52-9P 362665-53-0P 362665-54-1P, 3-Phenylpropyl
 3-piperidinopropyl ether 362665-55-2P 362665-56-3P,
 3-(4-Chlorophenyl)propyl 3-piperidinopropyl ether 362665-57-4P
362665-58-5P, 1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]piperidine
362665-63-2P 362665-66-5P, N-(6-Phenylhexyl)piperidine 362665-67-6P,
 N-(6-Phenylhexyl)piperidine hydrogen oxalate 362665-74-5P,
 3-(4-Chlorobenzyl)-5-(2-piperidinoethyl)-1,2,4-oxadiazole hydrogen oxalate
362665-81-4P, 3-Phenylpropyl 3-pyrrolidinopropyl ether 362665-82-5P
362665-85-8P 401805-28-5P, 1-[3-(4-Nitrophenoxy)propyl]-4-
 methylpiperidine 409127-50-0P, 2-Methyl-4-(3-
 piperidinopropylamino)quinoline 409127-54-4P, 7-Chloro-4-(4-
 piperidinobutylamino)quinoline 409127-57-7P, 4-(6-
 Piperidinoethylamino)quinoline 409127-58-8P, 2-Methyl-4-(6-
 piperidinoethylamino)quinoline 409127-62-4P, 7-Chloro-4-(8-
 piperidinoethylamino)quinoline 409127-63-5P, 7-Chloro-4-(10-
 piperidinodecylamino)quinoline 409127-84-0P, 10-Piperidinodecylamine
415936-57-1P, 1-[3-(4-Bromophenoxy)propyl]piperidine 462114-07-4P,
 3,3-Dimethylbutyl 3-piperidinopropyl ether 462114-09-6P 462114-10-9P
462114-65-4P 462114-66-5P 462114-67-6P 462114-68-7P,
 1-[3-(4-Cyanophenoxy)propyl]-4-methylpiperidine hydrochloride
462114-69-8P, 1-[3-(4-Cyanophenoxy)propyl]-3-methylpiperidine
 hydrochloride 462114-70-1P 462114-71-2P 462114-72-3P,
 1-[3-[4-(3-Oxobutyl)phenoxy]propyl]piperidine hydrochloride
462114-73-4P, 1-[3-(4-Cyano-3-fluorophenoxy)propyl]piperidine
 hydrochloride 462114-74-5P, 1-[3-(4-Nitrophenoxy)propyl]-3-
 methylpiperidine 462114-75-6P, 1-[3-(4-Nitrophenoxy)propyl]-3-
 methylpiperidine hydrogen oxalate 462114-76-7P, 1-[3-(4-
 Cyanophenoxy)propyl]-2-methylpiperidine hydrochloride 462114-77-8P,
 1-[3-(4-Nitrophenoxy)propyl]-2-methylpiperidine 462114-78-9P,
 1-[3-(4-Nitrophenoxy)propyl]-2-methylpiperidine hydrogen oxalate
462114-79-0P 462114-80-3P 462114-81-4P 462114-82-5P,
 1-[3-(4-Propionylphenoxy)propyl]-3-methylpiperidine hydrogen oxalate
462114-83-6P, 1-[3-[4-(Cyclobutylcarbonyl)phenoxy]propyl]piperidine
462114-84-7P 462114-85-8P, 1-[3-[4-(Cyclopentylcarbonyl)phenoxy]propyl]p-
 iperidine 462114-86-9P 462114-87-0P, 1-[3-(4-Cyanophenoxy)propyl]-cis-
 2-methyl-5-ethylpiperidine 462114-88-1P 462114-89-2P,
 1-[3-(4-Cyanophenoxy)propyl]-trans-2-methyl-5-ethylpiperidine

462114-90-5P 462114-91-6P, 1-[3-(4-Cyanophenoxy)propyl]-cis-3,5-dimethylpiperidine 462114-92-7P, 1-[3-(4-Cyanophenoxy)propyl]-cis-3,5-dimethylpiperidine hydrogen oxalate 462114-93-8P 462114-94-9P 462114-95-0P 462114-96-1P, 1-[3-(4-Propionylphenoxy)propyl]-2-methylpiperidine hydrogen oxalate 462114-97-2P, 1-[3-[4-(1-Hydroxypropyl)phenoxy]propyl]-3-methylpiperidine 462114-98-3P, 1-[3-[4-(1-Hydroxypropyl)phenoxy]propyl]-3-methylpiperidine hydrogen oxalate 462114-99-4P, 1-[3-[4-(1-Hydroxypropyl)phenoxy]propyl]-4-methylpiperidine 462115-00-0P, 1-[3-[4-(1-Hydroxypropyl)phenoxy]propyl]-4-methylpiperidine hydrogen oxalate 462115-01-1P, 1-[3-(4-Propionylphenoxy)propyl]-2-methylpiperidine oxime hydrochloride 462115-03-3P, 1-[3-(4-Propionylphenoxy)propyl]-4-methylpiperidine methoxime hydrogen oxalate 462115-04-4P, 1-[3-(4-Cyanophenoxy)propyl]-trans-3,5-dimethylpiperidine 462115-05-5P, 1-[3-(4-Cyanophenoxy)propyl]trans-3,5-dimethylpiperidine hydrogen oxalate 462115-06-6P, 1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]-trans-3,5-dimethylpiperidine 462115-07-7P, 1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]-trans-3,5-dimethylpiperidine hydrogen oxalate 462115-08-8P, 1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]-cis-3,5-dimethylpiperidine 462115-09-9P 462115-10-2P, 1-[3-(4-Carbomethoxyphenoxy)propyl]piperidine 462115-11-3P, 1-[3-(4-Carbomethoxyphenoxy)propyl]piperidine hydrogen oxalate 462115-12-4P 462115-13-5P 462115-14-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(H3 receptor modulator; prepn. of aryloxyalkylamines as histamine H3 receptor modulators)

IT 462115-15-7P, 1-[3-[4-(1-Ethoxypropyl)phenoxy]propyl]-2-methylpiperidine 462115-16-8P 462115-17-9P 462115-18-0P, 1-[3-(4-Propionylphenoxy)propyl]-4-methylpiperidine oxime hydrogen oxalate 462115-19-1P, 1-[3-(4-Bromophenoxy)propyl]piperidine hydrogen oxalate 462115-20-4P, 1-[3-(4-Nitrophenoxy)propyl]piperidine hydrogen oxalate 462115-22-6P 462115-23-7P 462115-24-8P, 1-[3-(4-Isopropylphenoxy)propyl]piperidine hydrogen oxalate 462115-25-9P, 1-[3-(4-sec-Butylphenoxy)propyl]piperidine 462115-26-0P 462115-27-1P 462115-28-2P, 1-[3-(4-Propylphenoxy)propyl]piperidine hydrogen oxalate 462115-29-3P 462115-30-6P, 1-[3-(4-Ethylphenoxy)propyl]piperidine hydrogen oxalate 462115-37-3P 462115-39-5P, 2-Benzothiazolyl 3-piperidinopropyl ether 462115-40-8P 462115-42-0P, 3-Cyclopentyl-N-[3-(1-pyrrolidinyl)propyl]propanamide 462115-43-1P, 3-Cyclopentyl-N-[3-(1-pyrrolidinyl)propyl]propanamide hydrogen oxalate 462115-44-2P 462115-45-3P 462115-46-4P 462115-47-5P 462115-48-6P 462115-49-7P 462115-50-0P 462115-51-1P 462115-54-4P, 5-Nitro-2-(6-piperidinohexyl)pyridine hydrogen oxalate 462115-56-6P, 3-Nitro-2-(6-piperidinohexylamino)pyridine 462115-57-7P, 3-Nitro-2-(6-piperidinohexylamino)pyridine hydrogen oxalate 462115-59-9P, 2-(6-Piperidinohexylamino)pyrimidine 462115-60-2P, 2-(6-Piperidinohexylamino)pyrimidine hydrogen oxalate 462115-61-3P 462115-62-4P 462115-63-5P 462115-64-6P 462115-65-7P 462115-66-8P 462115-67-9P 462115-68-0P 462115-69-1P 462115-70-4P 462115-71-5P 462115-72-6P 462115-73-7P 462115-74-8P 462115-75-9P 462115-76-0P 462115-77-1P 462115-78-2P 462115-79-3P 462115-80-6P 462115-81-7P 462115-82-8P 462115-83-9P 462115-84-0P 462115-85-1P 462115-86-2P 462115-87-3P 462115-88-4P, 4-(6-Piperidinohexylamino)quinoline dioxalate 462115-89-5P, 2-Methyl-4-(3-piperidinopropylamino)quinoline dioxalate 462115-90-8P, 2-Methyl-4-(6-piperidinohexylamino)quinoline dioxalate 462115-91-9P, 7-Chloro-4-(3-piperidinopropylamino)quinoline dioxalate 462115-92-0P, 7-Chloro-4-(4-piperidinobutylamino)quinoline dioxalate 462115-93-1P, 7-Chloro-4-(8-piperidinooctylamino)quinoline dioxalate 462115-94-2P, 7-Chloro-4-(10-piperidinodecylamino)quinoline dioxalate

462115-95-3P, 7-Chloro-4-(12-piperidinododecylamino)quinoline
462115-96-4P, 7-Chloro-4-(12-piperidinododecylamino)quinoline dioxalate
462115-97-5P, 7-Chloro-4-[[4-(3-piperidinopropoxy)phenyl]amino]quinoline
462115-98-6P, 7-Chloro-4-[[4-(3-piperidinopropoxy)phenyl]amino]quinoline dioxalate
462115-99-7P, 7-Chloro-4-[[2-[4-(3-piperidinopropoxy)phenyl]ethyl]amino]quinoline
462116-00-3P, 7-Chloro-4-[[2-[4-(3-piperidinopropoxy)phenyl]ethyl]amino]quinoline dioxalate
462116-01-4P 462116-02-5P 462116-03-6P,
 5-Nitro-2-(5-piperidinopentylamino)pyridine 462116-04-7P,
 5-Nitro-2-(5-piperidinopentylamino)pyridine hydrogen oxalate
462116-06-9P, 3-Nitro-2-(5-piperidinopentylamino)pyridine hydrogen oxalate
462116-07-0P, 5-Amino-2-(5-piperidinopentylamino)pyridine 462116-08-1P,
 5-Amino-2-(5-piperidinopentylamino)pyridine dioxalate 462116-09-2P,
 2-(6-Piperidinoethylamino)quinoline 462116-10-5P, 2-(6-Piperidinoethylamino)quinoline dioxalate
462116-11-6P 462116-12-7P,
 2-(6-Piperidinoethylamino)benzothiazole 462116-13-8P 462116-14-9P,
 10-Piperidinodecylamine dioxalate 462116-15-0P, 1-[3-(4-Cyanophenoxy)propyl]-4-methylpiperidine
462116-16-1P,
 1-[3-(4-Cyanophenoxy)propyl]-3-methylpiperidine 462116-17-2P,
 1-[3-(4-(3-Oxobutyl)phenoxy)propyl]piperidine 462116-18-3P,
 1-[3-(4-Cyano-3-fluorophenoxy)propyl]piperidine 462116-19-4P,
 1-[3-(4-Cyanophenoxy)propyl]-2-methylpiperidine 462116-20-7P,
 1-[3-(4-Cyanophenoxy)propyl]-2,6-dimethylpiperidine 462116-21-8P
462116-22-9P 462116-23-0P, 2-[(2-Piperidinoethyl)amino]benzothiazole
462116-24-1P, 2-Nitro-5-(6-piperidinoethyl)pyridine 462116-25-2P,
 N-Benzyl-N'-(3-piperidinopropyl)guanidine 462116-26-3P,
 N-Cyclohexylmethyl-N'-(3-piperidinopropyl)guanidine 462116-27-4P
462116-28-5P 462116-29-6P 462116-30-9P, N-(4-Bromobenzyl)-N'-(4-piperidinobutyl)sulfamide
462116-31-0P, 3-Chloro-N-(4-piperidinobutyl)-N-methylbenzenesulfonamide
462116-32-1P 462116-33-2P,
 cis-1-(6-Cyclohexyl-3-hexen-1-yl)piperidine 462116-34-3P,
 trans-1-(6-Cyclohexyl-3-hexen-1-yl)piperidine 462116-35-4P,
 1-[2-(5,5-Dimethyl-1-hexyn-1-yl)cyclopropyl]piperidine
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(H3 receptor modulator; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)

IT 24827-37-0P 54758-33-7P, (4-Hydroxyphenyl)cyclopentyl ketone
55154-90-0P 184031-01-4P, (4-Hydroxyphenyl)cyclobutyl ketone
462115-32-8P 462115-33-9P 462115-34-0P 462115-35-1P 462115-36-2P
462115-52-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)

IT 51-67-2, Tyramine 70-70-2, 4-Propionylphenol 86-98-6,
 4,7-Dichloroquinoline 98-59-9, p-Toluene sulfonyl chloride
99-93-4, 4'-Hydroxyacetophenone 103-71-9, Phenyl isocyanate, reactions
104-58-5, 3-(1-Piperidinyl)propanol 104-86-9, 4-Chlorobenzylamine
104-97-2, 3-Cyclopentylpropionyl chloride 108-91-8, Cyclohexylamine,
 reactions 108-95-2, Phenol, reactions 109-64-8, 1,3-Dibromopropane
109-89-7, Diethylamine, reactions 110-89-4, Piperidine, reactions
123-30-8, 4-Hydroxyaniline 123-75-1, Pyrrolidine, reactions 140-53-4,
 4-Chlorobenzyl cyanide 156-87-6, 3-Aminopropanol 504-63-2,
 1,3-Propanediol 532-55-8, Benzoyl isothiocyanate 588-63-6,
 3-Phenoxypropyl bromide 589-29-7, 1,4-Benzenedimethanol 611-35-8,
 4-Chloroquinoline 612-62-4, 2-Chloroquinoline 615-20-3,
 2-Chlorobenzothiazole 622-93-5 623-24-5 626-56-2, 3-Methylpiperidine
626-58-4, 4-Methylpiperidine 637-59-2, 3-Phenylpropyl bromide

765-38-8, 2-Methylpyrrolidine 772-31-6, Cyclopropyl 4-fluorophenyl ketone 1074-82-4, Potassium phthalimide 1122-82-3, Cyclohexyl isothiocyanate 1722-12-9, 2-Chloropyrimidine 2430-16-2, 6-Phenylhexanol 2508-29-4, 5-Aminopentanol 2528-61-2, n-Heptanoyl chloride 2855-08-5, 3,3-Dimethylbutyl chloride 3173-53-3, Cyclohexyl isocyanate 3344-70-5, 1,12-Dibromododecane 3694-45-9, 4-Chlorobenzylisothiocyanate 3954-13-0, Pentyl isocyanate 4048-33-3, 6-Aminohexanol 4101-68-2, 1,10-Dibromodecane 4295-06-1, 4-Chloro-2-methylquinoline 4524-93-0, Cyclopentylcarbonyl chloride 4548-45-2, 2-Chloro-5-nitropyridine 4549-32-0, 1,8-Dibromooctane 4897-50-1, 1,4'-Bipiperidine 5006-22-4, Cyclobutylcarbonyl chloride 5470-18-8, 2-Chloro-3-nitropyridine 5471-51-2, 4-(4-Hydroxyphenyl)-2-butanone 5472-49-1, N-(3-Chloropropyl)piperidine hydrochloride 6280-87-1, 5-Chlorovaleronitrile 13325-10-5, 4-Aminobutanol 22809-37-6, 6-Bromohexanoyl chloride 22921-72-8, 1-Bromo-5-phenoxy pentane 23159-07-1, 1-(3-Aminopropyl)pyrrolidine 23573-93-5, 27578-60-5, 1-Piperidineethanamine 35794-11-7, 3,5-Dimethylpiperidine 41903-50-8, Hydroxyacetophenone 61270-21-1, 4'-(5-Bromopentoxy)phenyl methyl ketone 61440-60-6, 3-(4-Chlorophenyl)propyl mesylate 65623-98-5, 4'-(3-Bromopropoxy)acetophenone 68453-37-2, 4-(Piperidinomethyl)benzoic acid methyl ester 69804-99-5, 3-Phenylpropylmesylate 93381-28-3, 3-Bromo-2-(R)-methyl-1-propanol 98244-48-5, 3-Bromo-2-(S)-methyl-1-propanol 134994-15-3, 1-Bromo-5-(4-benzoylphenoxy)pentane 362666-04-4, 3-Piperidinopropanol hydrochloride 462115-31-7, 4'-(5-Bromopentoxy)phenyl benzyl ketone 462115-38-4 462115-41-9
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reactant; prepn. of aryloxyalkylamines as **histamine** H3 receptor modulators)

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Full Text	Citing References
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AN 2002:736933 CAPLUS

DN 137:247603

TI Preparation of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer's** disease, ADHD, epilepsy, narcolepsy, and obesity

IN Bennani, Youssef L.; Faghih, Ramin; Dwight, Wesley J.; Vasudevan, Anil; Conner, Scott E.

PA USA

SO U.S. Pat. Appl. Publ., 62 pp., Cont.-in-part of U.S. Ser. No. 902,925.
 CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002137931	A1	20020926	US 2002-44471	20020111
	US 2002035103	A1	20020321	US 2001-902925	20010711
	US 6515013	B2	20030204		
PRAI	US 2000-218084P	P	20000713		
	US 2001-902925	A2	20010711		

OS MARPAT 137:247603

TI Preparation of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of **Alzheimer's** disease, ADHD, epilepsy, narcolepsy, and obesity

AB Title compds. I [wherein Z = a bond or CH₂; R₁ = OR₂, NR₃R₄, or 3-R₅-4-R₆-2,5-dioxoimidazolidinyl; R₂ = H, alkoxycarbonyl, alkyl(carbonyl), aminocarbonyl, sulfono, or phosphono; R₃ and R₄ =

independently H, alkenyl(sulfonyl), alkenyl(oxy)carbonyl, alkoxycarbonyl, alkyl(sulfonyl), alkylcarbonyl, aminocarbonyl, aminosulfonyl, alkynyl(sulfonyl), alkynyl(oxy)carbonyl, (un)substituted (hetero)arylalkyl, or (hetero)arylalkenylcarbonyl, etc.; R5, R6, and R7 = independently H or alkyl; or R1 and R7 together form =O; R8 = (cyclo)alkylcarbonyl, (un)substituted aryl(carbonyl), arylcarbonylaryl, arylcarbonylheterocyclyl, cycloalkylcarbonylaryl, cycloalkylcarbonylheterocyclyl, heterocyclyl(carbonyl), heterocyclylcarbonylaryl, or heterocyclylcarbonylheterocyclyl; R9 = H or alkyl; RA, RB, RC, and RD = independently H, alkenyl, alkoxy(alkoxy), (alkoxy)alkyl, alkoxycarbonyl, alkylcarbonyl(oxy), alkylsulfinyl, alkylsulfonyl, alkylthio, alkynyl, amino(alkyl), aminocarbonyl, (carboxy)alkyl, (cyano)alkyl, formyl, halo(alkoxy), haloalkyl, (hydroxy)alkyl, SH, or NO₂, etc.; and pharmaceutically acceptable salts] were prepd. as **histamine-3** receptor ligands. For example, 4'-[3-[(3R)-3-aminopyrrolidinyl]propoxy][1,1'-biphenyl]-4-carbonitrile in CH₂Cl₂ was treated with polymer supported N,N-diisopropylethylamine, catalytic amt. of DMAP, and 4-methoxybenzenesulfonyl chloride. After shaking at ambient temp. for 14 h, the mixt. was treated with tris(2-aminoethyl)amine-polystyrene resin and the mixt. shaken for an addnl. 2 h to give the [(biphenyloxy)propyl]pyrrolidinyl]benzenesulfonamide II (79%). The latter bound to the **histamine-3** receptor with K_i of 12 nM. I are useful for the treatment of acute myocardial infarction, asthma, bipolar disorder, cognitive enhancement, cutaneous carcinoma, depression, gastrointestinal disorders, inflammation, jet lag, medullary thyroid carcinoma, melanoma, Meniere's disease, migraine, motion sickness, obesity, pain, Parkinson's disease, schizophrenia, seizures, septic shock, Tourette's syndrome, Vertigo, wakefulness, **Alzheimer's** disease, attention-deficit hyperactivity disorder (ADHD), epilepsy, and narcolepsy (no data).

- ST aryloxypropylpyrrolidine prepn **histamine** receptor ligand;
biphenyloxypropylpyrrolidine prepn **Alzheimers** disease ADHD epilepsy
obesity narcolepsy treatment
- IT Sleep
(-waking cycle; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines
as **histamine-3** receptor ligands for treatment of
Alzheimer's disease, ADHD, epilepsy, narcolepsy, and obesity)
- IT. Brain, disease
(Gilles de la Tourette syndrome; prepn. of 1,3-di- and
1,3,3-trisubstituted pyrrolidines as **histamine-3** receptor
ligands for treatment of **Alzheimer's** disease, ADHD, epilepsy,
narcolepsy, and obesity)
- IT **Histamine** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(H3; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as
histamine-3 receptor ligands for treatment of **Alzheimer**
's disease, ADHD, epilepsy, narcolepsy, and obesity)
- IT Ear
(Meniere's disease, treatment; prepn. of 1,3-di- and
1,3,3-trisubstituted pyrrolidines as **histamine-3** receptor
ligands for treatment of **Alzheimer's** disease, ADHD, epilepsy,
narcolepsy, and obesity)
- IT Mental disorder
(attention deficit hyperactivity disorder, treatment; prepn. of 1,3-di-
and 1,3,3-trisubstituted pyrrolidines as **histamine-3** receptor
ligands for treatment of **Alzheimer's** disease, ADHD, epilepsy,
narcolepsy, and obesity)
- IT Rhythm, biological
(circadian, jet lag; prepn. of 1,3-di- and 1,3,3-trisubstituted
pyrrolidines as **histamine-3** receptor ligands for treatment of

- Alzheimer's disease, ADHD, epilepsy, narcolepsy, and obesity)**
- IT Mental disorder
(cognitive, psychiatric disorder; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine-3** receptor ligands for treatment of **Alzheimer's** disease, ADHD, epilepsy, narcolepsy, and obesity)
- IT Mental disorder
(depression; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine-3** receptor ligands for treatment of **Alzheimer's** disease, ADHD, epilepsy, narcolepsy, and obesity)
- IT Digestive tract
(disease; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine-3** receptor ligands for treatment of **Alzheimer's** disease, ADHD, epilepsy, narcolepsy, and obesity)
- IT Cognition
(disorder, psychiatric disorder; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine-3** receptor ligands for treatment of **Alzheimer's** disease, ADHD, epilepsy, narcolepsy, and obesity)
- IT Heart, disease
(infarction; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine-3** receptor ligands for treatment of **Alzheimer's** disease, ADHD, epilepsy, narcolepsy, and obesity)
- IT Mental disorder
(manic bipolar disorder; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine-3** receptor ligands for treatment of **Alzheimer's** disease, ADHD, epilepsy, narcolepsy, and obesity)
- IT Thyroid gland, neoplasm
(medullary carcinoma, treatment; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine-3** receptor ligands for treatment of **Alzheimer's** disease, ADHD, epilepsy, narcolepsy, and obesity)
- IT Headache
(migraine; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine-3** receptor ligands for treatment of **Alzheimer's** disease, ADHD, epilepsy, narcolepsy, and obesity)
- IT Sleep
(narcolepsy, treatment; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine-3** receptor ligands for treatment of **Alzheimer's** disease, ADHD, epilepsy, narcolepsy, and obesity)
-
- IT **Alzheimer's disease**
 Analgesics
 Anti-**Alzheimer's** agents
 Anti-inflammatory agents
 Antiasthmatics
 Anticonvulsants
 Antidepressants
 Antimigraine agents
 Antiobesity agents
 Antiparkinsonian agents
 Asthma
 Carcinoma
 Cardiovascular agents
 Cognition enhancers
 Dizziness
 Epilepsy
 Human
 Inflammation
 Melanoma
 Obesity

Parkinson's disease

Seizures

(prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as
histamine-3 receptor ligands for treatment of Alzheimer
's disease, ADHD, epilepsy, narcolepsy, and obesity)

IT Shock (circulatory collapse)

(septic, treatment; prepn. of 1,3-di- and 1,3,3-trisubstituted
pyrrolidines as histamine-3 receptor ligands for treatment of
Alzheimer's disease, ADHD, epilepsy, narcolepsy, and obesity)

IT Motion sickness

Schizophrenia

(treatment; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as
histamine-3 receptor ligands for treatment of Alzheimer
's disease, ADHD, epilepsy, narcolepsy, and obesity)

IT 392337-21-2P, 4'-[3-((3R)-3-Aminopyrrolidinyl)propoxy][1,1'-biphenyl]-4-
carbonitrile 392338-14-6P 392338-16-8P 392338-59-9P 392338-60-2P,
4'-[3-(3-Oxo-1-pyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
preparation); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); RACT (Reactant or reagent); USES (Uses)

(histamine-3 receptor ligand; prepn. of 1,3-di- and
1,3,3-trisubstituted pyrrolidines as histamine-3 receptor
ligands for treatment of Alzheimer's disease, ADHD, epilepsy,
narcolepsy, and obesity)

IT 392337-05-2P 392337-07-4P 392337-08-5P 392337-09-6P,
N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-2-(3-pyridinyl)-1,3-
thiazole-4-carboxamide 392337-10-9P 392337-11-0P, N-[(3R)-1-[3-(4-
Acetylphenoxy)propyl]pyrrolidinyl]-2-propanesulfonamide 392337-12-1P
392337-13-2P 392337-14-3P, (5S)-3'-[(3R)-1-[3-(4-
Acetylphenoxy)propyl]pyrrolidinyl]-5-methyl-2,4-imidazolidinedione
392337-15-4P 392337-16-5P, 4-Cyano-N-[(3R)-1-[3-(4-
(cyclopropylcarbonyl)phenoxy)propyl]pyrrolidinyl]benzenesulfonamide
392337-17-6P 392337-18-7P 392337-19-8P, N-[(3R)-1-[3-(4-
Acetylphenoxy)propyl]pyrrolidinyl]-4-cyanobenzamide 392337-20-1P
392337-22-3P 392337-23-4P 392337-24-5P 392337-25-6P 392337-26-7P,
N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-
methoxybenzenesulfonamide 392337-27-8P 392337-28-9P 392337-29-0P
392337-30-3P 392337-31-4P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-
yl)oxy]propyl]pyrrolidinyl]-2-methylbenzenesulfonamide 392337-32-5P,
3-Chloro-N-[(3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-
yl)oxy]propyl]pyrrolidinyl]-4-fluorobenzenesulfonamide 392337-33-6P
392337-34-7P 392337-35-8P 392337-36-9P 392337-37-0P,
3-Chloro-N-[(3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-
yl)oxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-38-1P
392337-39-2P 392337-40-5P 392337-41-6P 392337-42-7P,
N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-2-
thiophenesulfonamide 392337-43-8P 392337-44-9P 392337-45-0P
392337-46-1P 392337-47-2P, 4-Butoxy-N-[(3R)-1-[3-[(4'-cyano[1,1'-
biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-48-3P
392337-49-4P 392337-50-7P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-
yl)oxy]propyl]pyrrolidinyl]-2-phenylethanesulfonamide 392337-51-8P
392337-52-9P 392337-53-0P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-
yl)oxy]propyl]pyrrolidinyl]-3-methylbenzenesulfonamide 392337-54-1P
392337-55-2P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-
yl)oxy]propyl]pyrrolidinyl]-2,4-difluorobenzenesulfonamide 392337-56-3P
392337-57-4P 392337-58-5P, 3,4-Dichloro-N-[(3R)-1-[3-[(4'-cyano[1,1'-
biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-59-6P
392337-60-9P, 4-Bromo-N-[(3R)-1-[3-(4-(cyclopropylcarbonyl)phenoxy)propyl]
pyrrolidinyl]benzenesulfonamide 392337-61-0P 392337-62-1P
392337-63-2P, N-[(3R)-1-[3-(4-(Cyclopropylcarbonyl)phenoxy)propyl]pyrrolid

inyl]-4-methoxybenzenesulfonamide 392337-64-3P, 4-tert-Butyl-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-65-4P, N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-4-methylbenzenesulfonamide 392337-66-5P 392337-67-6P 392337-68-7P 392337-69-8P, 3-Chloro-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-4-fluorobenzenesulfonamide 392337-70-1P, N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-4-ethylbenzenesulfonamide 392337-71-2P 392337-72-3P 392337-73-4P 392337-74-5P, 3-Chloro-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-75-6P, 3-Cyano-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-76-7P, N-[(3R)-1-[3-[4-(4-Acetylphenoxy)propyl]pyrrolidinyl]-3-fluorobenzenesulfonamide 392337-77-8P 392337-78-9P 392337-79-0P, N-[(3R)-1-[3-[4-(4-Acetylphenoxy)propyl]pyrrolidinyl]-5-isoquinolinesulfonamide 392337-80-3P 392337-81-4P, N-[(3R)-1-[3-[4-(4-Acetylphenoxy)propyl]pyrrolidinyl]-3,4-dichlorobenzenesulfonamide 392337-82-5P 392337-84-7P, N-[(3R)-1-[3-[4-(4-Acetylphenoxy)propyl]pyrrolidinyl]-4-[[3-chloro-5-(trifluoromethyl)-2-pyridinyl]oxy]benzenesulfonamide 392337-85-8P 392337-86-9P, N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-2-thiophenesulfonamide 392337-87-0P 392337-88-1P 392337-89-2P, N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-8-quinolinesulfonamide 392337-90-5P 392337-92-7P 392337-93-8P 392337-94-9P, N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-2-phenylethanesulfonamide 392337-95-0P 392337-96-1P, 2-Cyano-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-97-2P 392337-98-3P 392337-99-4P 392338-00-0P 392338-01-1P 392338-02-2P, 3,4-Dichloro-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide 392338-03-3P 392338-04-4P 392338-05-5P 392338-06-6P 392338-08-8P 392338-09-9P 392338-10-2P 392338-11-3P 392338-12-4P, N-[2-Chloro-4-[[[(3R)-1-[3-[4-(2-pyridinyl)phenoxy]propyl]pyrrolidinyl]amino]sulfonyl]phenyl]acetamide 392338-13-5P, 4'-[3-[(3R)-3-(Dimethylamino)pyrrolidinyl]propoxy][1,1'-biphenyl]-4-carbonitrile 392338-17-9P 392338-18-0P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N,3,3-trimethylbutanamide 392338-19-1P 392338-20-4P 392338-21-5P 392338-22-6P 392338-23-7P, N'-tert-Butyl-N-[(3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N-methylurea 392338-24-8P 392338-25-9P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-fluoro-N-methylbenzamide 392338-26-0P 392338-27-1P 392338-28-2P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N-methyl-2-furamide 392338-29-3P 392338-30-6P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N,N',N'-trimethylsulfamide 392338-31-7P 392338-32-8P 392338-33-9P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-isopropyl-N-methylbenzenesulfonamide 392338-34-0P 392338-35-1P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-fluoro-N-(4-fluorobenzoyl)benzamide 392338-36-2P 392338-37-3P 392338-38-4P, Allyl (3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinylcarbamate 392338-39-5P, Methyl (3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinylcarbamate 392338-40-8P, tert-Pentyl (3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinylcarbamate 392338-41-9P 392338-42-0P 392338-43-1P 392338-44-2P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-morpholinecarboxamide 392338-45-3P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-fluorobenzamide 392338-46-4P 392338-47-5P 392338-48-6P 392338-49-7P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-

yl)oxy]propyl]pyrrolidinyl]-2-(3-pyridinyl)-1,3-thiazole-4-carboxamide
392338-50-0P 392338-51-1P, N'-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N,N-dimethylsulfamide 392338-52-2P
392338-53-3P 392338-54-4P 392338-55-5P 392338-56-6P,
 N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N-(4-morpholinylcarbonyl)-4-morpholinecarboxamide 392338-57-7P,
 Cyclopropyl[4-[3-(3-hydroxy-1-pyrrolidinyl)propoxy]phenyl]methanone
392338-58-8P 392338-61-3P 392338-62-4P, 4'-[3-(3-Hydroxy-3-methyl-1-pyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile 392338-63-5P,
 4'-[3-(3-Hydroxy-3-isopropyl-1-pyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile 392338-64-6P 392338-66-8P 392338-67-9P,
 N,N-Dimethyl-N-[(3S)-1-[3-[(4'-(1-pyrrolidinylcarbonyl)[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]amine 392338-68-0P 392338-69-1P
392338-71-5P 392338-72-6P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-3-fluorobenzenesulfonamide 392338-73-7P
461045-01-2P 461045-03-4P 461045-05-6P 461045-07-8P 461045-10-3P
461045-12-5P 461045-14-7P 461045-17-0P 461045-20-5P 461045-24-9P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(**histamine-3** receptor ligand; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine-3** receptor ligands for treatment of **Alzheimer's** disease, ADHD, epilepsy, narcolepsy, and obesity)

IT 36116-18-4P, Cyclopropyl(4-hydroxyphenyl)methanone 104582-67-4P
104582-73-2P 123843-58-3P 123864-93-7P, 3-Fluoro-4'-methoxy-1,1'-biphenyl-4-carbonitrile 133057-85-9P 149505-48-6P 149506-22-9P
360553-46-4P, [4-(3-Chloropropoxy)phenyl](cyclopropyl)methanone
392337-06-3P, 1-[4-[3-((3R)-3-Aminopyrrolidinyl)propoxy]phenyl]ethanone
392338-07-7P, (3R)-1-[3-[4-(2-Pyridinyl)phenoxy]propyl]pyrrolidinylamine
460746-47-8P 460748-04-3P 460748-08-7P 461045-02-3P 461045-04-5P
461045-06-7P 461045-08-9P 461045-09-0P 461045-11-4P 461045-13-6P
461045-15-8P 461045-16-9P 461045-18-1P 461045-19-2P 461045-21-6P
461045-23-8P 461045-25-0P 461045-26-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine-3** receptor ligands for treatment of **Alzheimer's** disease, ADHD, epilepsy, narcolepsy, and obesity)

IT 59-67-6, Nicotinic acid, reactions 70-70-2, 1-(4-Hydroxyphenyl)-1-propanone 79-44-7, Dimethylcarbamy l chloride 98-09-9, Benzenesulfonyl chloride 98-68-0, 4-Methoxybenzenesulfonyl chloride 99-93-4, 1-(4-Hydroxyphenyl)ethanone 109-70-6, 1-Bromo-3-chloropropane 133-59-5, 2-Methylbenzenesulfonyl chloride 403-43-0, 4-Fluorobenzoyl chloride 527-69-5, 2-Furoyl chloride 619-65-8, 4-Cyanobenzoic acid 701-27-9, 3-Fluorobenzenesulfonyl chloride 1068-55-9, Isopropylmagnesium chloride 1138-56-3, 4-Butoxybenzenesulfonyl chloride 1192-63-8, 1-Pyrrolidinecarbonyl chloride 1759-53-1, Cyclopropanecarboxylic acid 2105-94-4, 4-Bromo-2-fluorophenol 2362-12-1, 4-Bromo-2-methylphenol 2799-21-5 2937-50-0, Allyl chloroformate 3794-80-7, 1,1-Dimethylpropyl chloroformate 3964-56-5, 4-Bromo-2-chlorophenol 5720-07-0, 4-Methoxyphenylboronic acid 6068-72-0, 4-Cyanobenzoyl chloride 7065-46-5, tert-Butylacetyl chloride 7150-55-2 7368-78-7, 4-Bromo-2-methoxyphenol 7764-95-6, (2R)-2-[(tert-Butoxycarbonyl)amino]propanoic acid 10147-37-2, 2-Propanesulfonyl chloride 10400-19-8, Nicotinoyl chloride 13360-57-1, Dimethylsulfamoyl chloride 14472-14-1, 4-Bromo-3-methylphenol 15159-40-7, 4-Morpholinecarbonyl chloride 15761-38-3, (2S)-2-[(tert-Butoxycarbonyl)amino]propanoic acid 19812-93-2, 4'-Hydroxy[1,1'-biphenyl]-4-carbonitrile 39067-29-3, 2-(3-Pyridinyl)-1,3-thiazole-4-

carboxylic acid 40499-83-0, 3-Hydroxypyrrolidine 41891-21-8,
 tert-Butylcarbonyl chloride 41963-20-6, 4-Bromo-3-methylbenzonitrile
46118-95-0, [(4-Methyl-2-pyrimidinyl)sulfonyl]acetic acid 49584-26-1,
 4-Cyanobenzenesulfonyl chloride 51035-40-6, 4-(2-Pyridinyl)phenol
56542-67-7, 3-Cyanobenzenesulfonyl chloride 67832-11-5,
 4-Bromo-2-methylbenzonitrile 68835-89-2, Di(tert-pentyl) dicarbonate
71530-58-0 82964-91-8, 4-(Methylsulfonyl)benzenesulfonyl chloride
94108-56-2, 4-(Trifluoromethoxy)benzenesulfonyl chloride 100243-39-8,
 (3S)-3-Pyrrolidinol 104197-13-9, 4-Bromo-2,6-difluorophenol
105942-08-3, 4-Bromo-2-fluorobenzonitrile 122536-77-0 126747-14-6,
 4-Cyanophenylboronic acid 132883-44-4, N,N-Dimethyl-N-((3S)-
 pyrrolidinyl)amine 132958-72-6, N,N-Dimethyl-N-((3R)-pyrrolidinyl)amine
161045-79-0 180992-31-8, 2-(3-Pyridinyl)-1,3-thiazole-4-carbonyl
 chloride 372514-08-4, 1-[[4'-(3-Chloropropoxy)[1,1'-biphenyl]-4-
 yl]carbonyl]pyrrolidine 392337-91-6, [4-[3-((3R)-3-
 Aminopyrrolidinyl)propoxy]phenyl](cyclopropyl)methanone 392338-15-7
392338-65-7, (3R)-3-Methyl-3-pyrrolidinol 392338-70-4,
 1-[4-(3-Chloropropoxy)phenyl]-4-(1-pyrrolidinylcarbonyl)piperazine
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reactant; prepn. of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as
histamine-3 receptor ligands for treatment of **Alzheimer**
 's disease, ADHD, epilepsy, narcolepsy, and obesity)

L8 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS

Full Text	Citing References
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AN 2002:221215 CAPLUS

DN 136:263087

TI Preparation of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as
histamine-3 receptor ligands for treatment of **Alzheimer's** disease,
 ADHD, epilepsy, and narcolepsy

IN Bennani, Youssef L.; Faghih, Ramin; Dwight, Wesley J.; Vasudevan, Anil;
 Conner, Scott E.

PA USA

SO U.S. Pat. Appl. Publ., 54 pp.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US <u>2002035103</u>	A1	20020321	US <u>2001-902925</u>	20010711
	US <u>6515013</u>	B2	20030204		
	US <u>2002137931</u>	A1	20020926	US <u>2002-44471</u>	20020111
PRAI	US <u>2000-218084P</u>	P	20000713		
	US <u>2001-902925</u>	A2	20010711		

OS MARPAT 136:263087

TI Preparation of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as
histamine-3 receptor ligands for treatment of **Alzheimer's** disease,
 ADHD, epilepsy, and narcolepsy

AB Title compds. I [wherein Z = a bond or CH₂; R₁ = OR₂, NR₃R₄, or
 substituted 2,5-dioxoimidazolidinyl; R₂ = H, alkoxycarbonyl,
 alkyl(carbonyl), aminocarbonyl, sulfono, or phosphono; R₃ and R₄ =
 independently H, alkenyl(sulfonyl), alkenyl(oxy)carbonyl, alkoxycarbonyl,
 alkyl(sulfonyl), alkylcarbonyl, aminocarbonyl, aminosulfonyl,
 alkynyl(sulfonyl), alkynyl(oxy)carbonyl, or (un)substituted
 (hetero)arylalkyl, (hetero)arylalkenylcarbonyl, etc.; R₇ = H or alkyl; or
 R₁ and R₇ together form :O; R₈ = (cyclo)alkylcarbonyl, or (un)substituted
 aryl(carbonyl), arylcarbonylaryl, arylcarbonylheterocyclyl,
 cycloalkylcarbonylaryl, cycloalkylcarbonylheterocyclyl,

heterocyclyl(carbonyl), heterocyclylcarbonylaryl, or heterocyclylcarbonylheterocyclyl; R9 = H or alkyl] were prepd. as **histamine-3** receptor ligands. For example, 4'-[3-[(3R)-3-aminopyrrolidinyl]propoxy][1,1'-biphenyl]-4-carbonitrile in CH₂Cl₂ was treated with polymer supported N,N-diisopropylethylamine, catalytic N,N-dimethylaminopyridine, and 4-methoxybenzenesulfonyl chloride. After shaking at ambient temp. for 14 h, the mixt. was treated with tris(2-aminoethyl)amine-polystyrene resin and the mixt. shaken for an addnl. 2 h to give the [[(biphenyloxy)propyl]pyrrolidinyl]benzenesulfonamide II (79%). The latter bound to the **histamine-3** receptor with K_i of 12 nM. I are useful for the treatment of acute myocardial infarction, asthma, cutaneous carcinoma, depression, inflammation, medullary thyroid carcinoma, melanoma, Meniere's disease, migraine, motion sickness, obesity, pain, Parkinson's disease, schizophrenia, seizures, septic shock, **Alzheimer's** disease, attention-deficit hyperactivity disorder (ADHD), epilepsy, and narcolepsy.

- ST aryloxypropyl pyrrolidine prepn **histamine** receptor ligand;
biphenyloxypropyl pyrrolidine prepn **Alzheimers** disease ADHD epilepsy
narcolepsy treatment
- IT **Histamine** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(H3; prepn. of di- and trisubstituted pyrrolidines as **histamine**
-3 receptor ligands for treatment of **Alzheimer's** disease,
ADHD, epilepsy, and narcolepsy)
- IT Ear
(Meniere's disease, treatment; prepn. of di- and trisubstituted
pyrrolidines as **histamine-3** receptor ligands for treatment of
Alzheimer's disease, ADHD, epilepsy, and narcolepsy)
- IT Mental disorder
(attention deficit hyperactivity disorder, treatment; prepn. of di- and
trisubstituted pyrrolidines as **histamine-3** receptor ligands
for treatment of **Alzheimer's** disease, ADHD, epilepsy, and
narcolepsy)
- IT Antitumor agents
(carcinoma; prepn. of di- and trisubstituted pyrrolidines as
histamine-3 receptor ligands for treatment of **Alzheimer**
's disease, ADHD, epilepsy, and narcolepsy)
- IT Heart, disease
(infarction, therapeutic agents; prepn. of di- and trisubstituted
pyrrolidines as **histamine-3** receptor ligands for treatment of
Alzheimer's disease, ADHD, epilepsy, and narcolepsy)
- IT Thyroid gland, neoplasm
(medullary carcinoma, treatment; prepn. of di- and trisubstituted
pyrrolidines as **histamine-3** receptor ligands for treatment of
Alzheimer's disease, ADHD, epilepsy, and narcolepsy)
- IT Antitumor agents
(melanoma; prepn. of di- and trisubstituted pyrrolidines as
histamine-3 receptor ligands for treatment of **Alzheimer**
's disease, ADHD, epilepsy, and narcolepsy)
- IT Sleep
(narcolepsy, treatment; prepn. of di- and trisubstituted pyrrolidines
as **histamine-3** receptor ligands for treatment of
Alzheimer's disease, ADHD, epilepsy, and narcolepsy)
- IT Analgesics
Anti-**Alzheimer's** agents
Anti-inflammatory agents
Antiasthmatics
Anticonvulsants
Antidepressants
Antimigraine agents

Antiobesity agents
 Antiparkinsonian agents
 Human

(prepn. of di- and trisubstituted pyrrolidines as **histamine-3** receptor ligands for treatment of **Alzheimer's** disease, ADHD, epilepsy, and narcolepsy)

IT Shock (circulatory collapse)

(septic, treatment; prepn. of di- and trisubstituted pyrrolidines as **histamine-3** receptor ligands for treatment of **Alzheimer's** disease, ADHD, epilepsy, and narcolepsy)

IT Motion sickness

Schizophrenia

(treatment; prepn. of di- and trisubstituted pyrrolidines as **histamine-3** receptor ligands for treatment of **Alzheimer's** disease, ADHD, epilepsy, and narcolepsy)

IT 392337-21-2P, 4'-[3-((3R)-3-Aminopyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile 392338-14-6P 392338-16-8P 392338-59-9P 392338-60-2P, 4'-[3-(3-Oxo-1-pyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(**histamine-3** receptor ligand; prepn. of di- and trisubstituted pyrrolidines as **histamine-3** receptor ligands for treatment of **Alzheimer's** disease, ADHD, epilepsy, and narcolepsy)

IT 392337-05-2P 392337-07-4P 392337-08-5P 392337-09-6P, N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-2-(3-pyridinyl)-1,3-thiazole-4-carboxamide 392337-10-9P 392337-11-0P, N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-2-propanesulfonamide 392337-12-1P 392337-13-2P 392337-14-3P, (5S)-3-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-5-methyl-2,4-imidazolidinedione 392337-15-4P 392337-16-5P, 4-Cyano-N-[(3R)-1-[3-(4-(cyclopropylcarbonyl)phenoxy)propyl]pyrrolidinyl]benzenesulfonamide 392337-17-6P 392337-18-7P 392337-19-8P, N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-4-cyanobenzamide 392337-20-1P 392337-22-3P 392337-23-4P 392337-24-5P 392337-25-6P 392337-26-7P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-methoxybenzenesulfonamide 392337-27-8P 392337-28-9P 392337-29-0P 392337-30-3P 392337-31-4P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-2-methylbenzenesulfonamide 392337-32-5P, 3-Chloro-N-[(3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-fluorobenzenesulfonamide 392337-33-6P 392337-34-7P 392337-35-8P 392337-36-9P 392337-37-0P, 3-Chloro-N-[(3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-38-1P 392337-39-2P 392337-40-5P 392337-41-6P 392337-42-7P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-2-thiophenesulfonamide 392337-43-8P 392337-44-9P 392337-45-0P 392337-46-1P 392337-47-2P, 4-Butoxy-N-[(3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-48-3P 392337-49-4P 392337-50-7P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-2-phenylethanesulfonamide 392337-51-8P 392337-52-9P 392337-53-0P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-3-methylbenzenesulfonamide 392337-54-1P 392337-55-2P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-2,4-difluorobenzenesulfonamide 392337-56-3P 392337-57-4P 392337-58-5P, 3,4-Dichloro-N-[(3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-59-6P 392337-60-9P, 4-Bromo-N-[(3R)-1-[3-(4-(cyclopropylcarbonyl)phenoxy)propyl]pyrrolidinyl]benzenesulfonamide 392337-61-0P 392337-62-1P

392337-63-2P, N-[(3R)-1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-4-methoxybenzenesulfonamide 392337-64-3P, 4-tert-Butyl-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide
 392337-65-4P, N-[(3R)-1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-4-methylbenzenesulfonamide 392337-66-5P 392337-67-6P
 392337-68-7P 392337-69-8P, 3-Chloro-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-4-fluorobenzenesulfonamide 392337-70-1P, N-[(3R)-1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-4-ethylbenzenesulfonamide 392337-71-2P 392337-72-3P 392337-73-4P
 392337-74-5P, 3-Chloro-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-75-6P, 3-Cyano-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide
 392337-76-7P, N-[(3R)-1-[3-[4-(4-Acetylphenoxy)propyl]pyrrolidinyl]-3-fluorobenzenesulfonamide 392337-77-8P 392337-78-9P 392337-79-0P, N-[(3R)-1-[3-[4-(4-Acetylphenoxy)propyl]pyrrolidinyl]-5-isoquinolinesulfonamide 392337-80-3P 392337-81-4P, N-[(3R)-1-[3-[4-(4-Acetylphenoxy)propyl]pyrrolidinyl]-3,4-dichlorobenzenesulfonamide 392337-82-5P 392337-84-7P, N-[(3R)-1-[3-[4-(4-Acetylphenoxy)propyl]pyrrolidinyl]-4-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]oxy]benzenesulfonamide 392337-85-8P
 392337-86-9P, N-[(3R)-1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-2-thiophenesulfonamide 392337-87-0P 392337-88-1P 392337-89-2P, N-[(3R)-1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-8-quinolinesulfonamide 392337-90-5P 392337-92-7P 392337-93-8P
 392337-94-9P, N-[(3R)-1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-2-phenylethanesulfonamide 392337-95-0P 392337-96-1P, 2-Cyano-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide 392337-97-2P 392337-98-3P 392337-99-4P
 392338-00-0P 392338-01-1P 392338-02-2P, 3,4-Dichloro-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide 392338-03-3P 392338-04-4P 392338-05-5P 392338-06-6P 392338-08-8P
 392338-09-9P 392338-10-2P 392338-11-3P 392338-12-4P, N-[2-Chloro-4-[[[(3R)-1-[3-[4-(2-pyridinyl)phenoxy]propyl]pyrrolidinyl]amino]sulfonyl]phenyl]acetamide 392338-13-5P, 4'-[3-[(3R)-3-(Dimethylamino)pyrrolidinyl]propoxy][1,1'-biphenyl]-4-carbonitrile 392338-17-9P 392338-18-0P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N,3,3-trimethylbutanamide 392338-19-1P 392338-20-4P 392338-21-5P 392338-22-6P 392338-23-7P, N'-tert-Butyl-N-[(3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N-methylurea 392338-24-8P 392338-25-9P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-fluoro-N-methylbenzamide 392338-26-0P 392338-27-1P 392338-28-2P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N-methyl-2-furamide 392338-29-3P 392338-30-6P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N,N',N'-trimethylsulfamide 392338-31-7P 392338-32-8P 392338-33-9P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-isopropyl-N-methylbenzenesulfonamide 392338-34-0P 392338-35-1P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-fluoro-N-(4-fluorobenzoyl)benzamide 392338-36-2P 392338-37-3P
 392338-38-4P, Allyl (3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinylcarbamate 392338-39-5P, Methyl (3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinylcarbamate 392338-40-8P, tert-Pentyl (3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinylcarbamate 392338-41-9P 392338-42-0P
 392338-43-1P 392338-44-2P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-morpholinecarboxamide 392338-45-3P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-fluorobenzamide 392338-46-4P 392338-47-5P 392338-48-6P

392338-49-7P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-2-(3-pyridinyl)-1,3-thiazole-4-carboxamide
 392338-50-0P 392338-51-1P, N'-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N,N-dimethylsulfamide 392338-52-2P
 392338-53-3P 392338-54-4P 392338-55-5P 392338-56-6P,
 N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N-(4-morpholinylcarbonyl)-4-morpholinecarboxamide 392338-57-7P
 392338-58-8P, Cyclopropyl[4-[3-((3R)-3-hydroxypyrrolidinyl)propoxy]phenyl]methanone 392338-61-3P, 4'-[3-((3S)-3-Hydroxypyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile 392338-62-4P, 4'-[3-(3-Hydroxy-3-methyl-1-pyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile 392338-63-5P, 4'-[3-(3-Hydroxy-3-isopropyl-1-pyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile 392338-64-6P, 4'-[3-((3R)-3-Hydroxy-3-methylpyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile 392338-66-8P
 392338-67-9P, N,N-Dimethyl-N-[(3S)-1-[3-[(4'-((1-pyrrolidinylcarbonyl)[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]amine 392338-68-0P 392338-69-1P
 392338-71-5P 392338-72-6P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-3-fluorobenzenesulfonamide 392338-73-7P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(histamine-3 receptor ligand; prepn. of di- and trisubstituted pyrrolidines as histamine-3 receptor ligands for treatment of Alzheimer's disease, ADHD, epilepsy, and narcolepsy)

IT 36116-18-4P, Cyclopropyl(4-hydroxyphenyl)methanone 360553-46-4P, [4-(3-Chloropropoxy)phenyl](cyclopropyl)methanone 392337-06-3P, 1-[4-[3-[(3R)-3-Aminopyrrolidinyl]propoxy]phenyl]ethanone 392338-07-7P, (3R)-1-[3-[4-(2-Pyridinyl)phenoxy]propyl]pyrrolidinylamine
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; prepn. of di- and trisubstituted pyrrolidines as histamine-3 receptor ligands for treatment of Alzheimer's disease, ADHD, epilepsy, and narcolepsy)

IT 59-67-6, Nicotinic acid, reactions 70-70-2, 1-(4-Hydroxyphenyl)-1-propanone 79-44-7, Dimethylcarbamyloxy chloride 98-09-9, Benzenesulfonyl chloride 98-68-0, 4-Methoxybenzenesulfonyl chloride 99-93-4, 1-(4-Hydroxyphenyl)ethanone 109-70-6, 1-Bromo-3-chloropropane 133-59-5, 2-Methylbenzenesulfonyl chloride 403-43-0, 4-Fluorobenzoyl chloride 527-69-5, 2-Furoyl chloride 619-65-8, 4-Cyanobenzoic acid 701-27-9, 3-Fluorobenzenesulfonyl chloride 1068-55-9, Isopropylmagnesium chloride 1138-56-3, 4-Butoxybenzenesulfonyl chloride 1192-63-8, 1-Pyrrolidinecarbonyl chloride 1759-53-1, Cyclopropanecarboxylic acid 2799-21-5, 3-(3R)-Hydroxypyrrolidine 2937-50-0, Allyl chloroformate 3794-80-7, 1,1-Dimethylpropyl chloroformate 6068-72-0, 4-Cyanobenzoyl chloride 7065-46-5, tert-Butylacetyl chloride 7150-55-2 7764-95-6, (2R)-2-[(tert-Butoxycarbonyl)amino]propanoic acid 10147-37-2, 2-Propanesulfonyl chloride 10400-19-8, Nicotinoyl chloride 13360-57-1, Dimethylsulfamoyl chloride 15159-40-7, 4-Morpholinecarbonyl chloride 15761-38-3, (2S)-2-[(tert-Butoxycarbonyl)amino]propanoic acid 19812-93-2, 4'-Hydroxy[1,1'-biphenyl]-4-carbonitrile 39067-29-3, 2-(3-Pyridinyl)-1,3-thiazole-4-carboxylic acid 40499-83-0, 3-Hydroxypyrrolidine 41891-21-8, tert-Butylcarbamoxy chloride 46118-95-0, [(4-Methyl-2-pyrrolidinyl)sulfonyl]acetic acid 49584-26-1, 4-Cyanobenzenesulfonyl chloride 51035-40-6, 4-(2-Pyridinyl)phenol 56542-67-7, 3-Cyanobenzenesulfonyl chloride 68835-89-2, Di(tert-pentyl)dicarbonate 71530-58-0 82964-91-8, 4-(Methylsulfonyl)benzenesulfonyl chloride 94108-56-2, 4-(Trifluoromethoxy)benzenesulfonyl chloride 100243-39-8, (3S)-3-Pyrrolidinol 122536-77-0 132883-44-4, N,N-Dimethyl-N-((3S)-pyrrolidinyl)amine 132958-72-6,

N,N-Dimethyl-N-((3R)-pyrrolidinyl)amine 180992-31-8,
 2-(3-Pyridinyl)-1,3-thiazole-4-carbonyl chloride 372514-08-4,
 1-[[4'-(3-Chloropropoxy)[1,1'-biphenyl]-4-yl]carbonyl]pyrrolidine
392337-91-6, [4-{3-((3R)-3-Aminopyrrolidinyl)propoxy]phenyl] (cyclopropyl)m
 ethanone 392338-15-7 392338-65-7, (3R)-3-Methyl-3-pyrrolidinol
392338-70-4, 1-[4-(3-Chloropropoxy)phenyl]-4-(1-
 pyrrolidinylcarbonyl)piperazine
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reactant; prepn. of di- and trisubstituted pyrrolidines as
histamine-3 receptor ligands for treatment of **Alzheimer**
 's disease, ADHD, epilepsy, and narcolepsy)

=> d his

(FILE 'HOME' ENTERED AT 06:05:56 ON 20 JUN 2003)

FILE 'CAPLUS' ENTERED AT 06:06:21 ON 20 JUN 2003
 E DEMENTIA/CT

FILE 'CAPLUS, WPIDS, MEDLINE, EMBASE' ENTERED AT 06:07:28 ON 20 JUN 2003

L1 172320 S DEMENTIA OR ALZHEIMER?
 L2 182615 S L1 OR NEURODEGENERAT? DISEASE#
 L3 1127914 S ((SULFONYLAMIDO OR SULFONYL AMIDO) (2A) HISTAMINE) OR NSAID O
 L4 3550 S L2 (L) L3
 L5 0 S L4 AND ((SULFONYLAMIDO (5A) HISTAMINE) OR (SULFONYL (5A) AMI
 L6 24 S L4 AND HISTAMINE
 L7 496 S L2 AND HISTAMINE
 L8 3 S L7 AND (HISTAMINE (10A) SULFONYL)

=> file reg

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	100.95	101.99
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
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CA SUBSCRIBER PRICE	-1.95	-1.95

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 DICTIONARY FILE UPDATES: 18 JUN 2003 HIGHEST RN 533863-98-8

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

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Experimental and calculated property data are now available. See HELP
PROPERTIES for more information. See STNnote 27, Searching Properties
 in the CAS Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> s histamine and (sulfonyl (3a) amido)

484 HISTAMINE

862550 SULFONYL

89443 AMIDO

2885 SULFONYL (3A) AMIDO

L9 0 HISTAMINE AND (SULFONYL (3A) AMIDO)

=> s histamine and sulfonyl

484 HISTAMINE

862550 SULFONYL

L10 0 HISTAMINE AND SULFONYL

=> s histamine and sulfon?

484 HISTAMINE

1441970 SULFON?

L11 0 HISTAMINE AND SULFON?

=> s histamine and sulfo?

484 HISTAMINE

1539676 SULFO?

L12 0 HISTAMINE AND SULFO?

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

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FULL ESTIMATED COST

39.58

141.57

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FILE COVERS 1907 - 20 Jun 2003 VOL 138 ISS 26

FILE LAST UPDATED: 19 Jun 2003 (20030619/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s sulfonylamido (5a) histamine/ab

57 SULFONYLAMIDO

49170 HISTAMINE/AB

L13 1 SULFONYLAMIDO (5A) HISTAMINE/AB

=> d hit

L13 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS

Citing References

AB **Sulfonylamido**(ureido) derivs. of **histamine** were synthesized by an original procedure in order to obtain tight-binding activators of the zinc enzyme carbonic anhydrase (CA), exploiting the binding energy of the alkyl/arylsulfonyl moieties with amino acid residues at the entrance of the active site. In contrast to the lead mol., histamine, the new derivs. possessed higher affinity for three different CA isoenzymes, as evidenced by comparing the affinity consts. of these compds. for isoenzyme CA II.

=> d bib

L13 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS

Full Text	Citing References
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AN 1999:504279 CAPLUS
 DN 131:286325
 TI Novel carbonic anhydrase isozymes I, II and IV activators incorporating sulfonyl-histamino moieties
 AU Briganti, Fabrizio; Scozzafava, Andrea; Supuran, Claudiu T.
 CS Universita degli Studi, Laboratorio di Chimica Inorganica e Bioinorganica, Florence, 50121, Italy
 SO Bioorganic & Medicinal Chemistry Letters (1999), 9(14), 2043-2048
 CODEN: BMCLE8; ISSN: 0960-894X
 PB Elsevier Science Ltd.
 DT Journal
 LA English
 RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d bib ab

L13 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS

Full Text	Citing References
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 DN 131:286325
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 SO Bioorganic & Medicinal Chemistry Letters (1999), 9(14), 2043-2048
 CODEN: BMCLE8; ISSN: 0960-894X
 PB Elsevier Science Ltd.
 DT Journal
 LA English
 AB **Sulfonylamido**(ureido) derivs. of **histamine** were synthesized by an original procedure in order to obtain tight-binding activators of the zinc enzyme carbonic anhydrase (CA), exploiting the binding energy of the alkyl/arylsulfonyl moieties with amino acid residues at the entrance of the active site. In contrast to the lead mol., histamine, the new derivs. possessed higher affinity for three different CA isoenzymes, as evidenced by comparing the affinity consts. of these compds. for isoenzyme CA II.

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>

AN 2000:575630 CAPLUS
 DN 133:129891
 TI Medicine for treating senility dementia, parkinsonism and cardiocerebral
 angiopathy
 IN Lu, Gao
 PA Peop. Rep. China
 SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 14 pp.
 CODEN: CNXXEV
 DT Patent
 LA Chinese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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<u>PI</u>	CN 1228995	A	19990922	CN 1999-113434	19990126
<u>PRAI</u>	CN 1999-113434		19990126		

AB One or more of nerve growth factor, brain-derived neurotrophic factor,
 nerve trophic factor-3, nerve trophic factor-4, nerve trophic factor-5,
 ciliary neurotrophic factor, fibroblast growth factor, epidermal growth
 factor, ganglioside, acetylcholine, histamine, calcitonin gene-related
 peptide, neuropeptide, cAMP, atrial natriuretic peptide, brain natriuretic
 peptide, C-type natriuretic peptide, PGI₂, and EDRF are used for treatment
 of senility dementia, parkinsonism, cardiocerebral angiopathy, coronary
 heart disease, hypertension, and atheromatosis.

AN 1997:759697 CAPLUS
DN 128:60291
TI Neuronal histamine deficit in Alzheimer's disease
AU Panula, P.; Rinne, J.; Kuokkanen, K.; Eriksson, K. S.; Sallmen, T.;
Kalimo, H.; Relja, M.
CS Department of Biology, Abo Akademi University, Turku, FIN-20520, Finland
SO Neuroscience (Oxford) (1997), Volume Date 1998, 82(4), 993-997
CODEN: NRSCDN; ISSN: 0306-4522
PB Elsevier Science Ltd.
DT Journal
LA English
AB Histamine is known to be a neurotransmitter in the brain, but it has not been clearly implicated in major diseases. All histaminergic neurons reside in the posterior hypothalamus and innervate most brain areas, which is compatible with the concept that histamine is involved in general central regulatory mechanisms. A sensitive, high-performance liq. chromatog. fluorimetric method was used to measure histamine contents in post mortem Alzheimer brains and age-matched controls. The cellular storage sites and distribution of histaminergic nerve fibers were examd. with a specific immunohistochem. method. The histamine content was reduced in the hypothalamus (42% of control value), hippocampus (43%) and temporal cortex (53%) of Alzheimer brains. Differences in other cortical areas, putamen, and substantia nigra were not significant. Histamine-contg. nerve fibers were found in the hippocampus, parahippocampal gyrus, and subiculum of both Alzheimer brains and controls. No histamine-contg. mast cells were seen in these temporal structures. Histamine in the human temporal lobe is stored in nerve fibers originating from the posterior hypothalamus, and not in mast cells. Decrease in brain histamine may contribute to the cognitive decline in Alzheimer's disease directly or through the cholinergic system. Development of drugs that penetrate the blood-brain barrier and increase histaminergic activity might be beneficial in Alzheimer's disease.

AN 1997:110225 CAPLUS
DN 126:223838
TI Similar deficits of central histaminergic system in patients with Down syndrome and Alzheimer disease
AU Schneider, Christoph; Risser, Daniele; Kirchner, Liselotte; Kitzmueller, Erwin; Cairns, Nigel; Prast, Helmut; Singewald, Nicolas; Lubec, Gert
CS Department of Pediatrics, University of Vienna, A 1090, Vienna, Austria
SO Neuroscience Letters (1997), 222(3), 183-186
CODEN: NELED5; ISSN: 0304-3940
PB Elsevier
DT Journal
LA English
AB To study whether Alzheimer-like neuropathol. changes involve the central histaminergic system, the authors measured the concn. of histamine, its precursor histidine, and the activities of histidine decarboxylase (HDC) and histamine N-methyltransferase (HMT) in frontal cortex of aging Down syndrome (DS) patients, Alzheimer patients, and control individuals. The study populations were also investigated for choline acetyltransferase (ChAT) activity, since reduced ChAT activity is an established biochem. hallmark in DS and Alzheimer disease (AD). HDC and ChAT activity were reduced in brains of both DS and Alzheimer patients vs. control patients. Addnl., the authors obsd. a significant decrease of histamine levels in the DS group. Histamine levels in AD brains tended to be decreased. Histidine concns. and HMT activities were comparable between the three groups. Thus, the authors' results for the first time show histaminergic deficits in brains of patients with DS resembling the neurochem. pattern in AD. Neuropathol. changes may be responsible for similar neurochem. alterations of the histaminergic system in both dementing disorders.